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COMPARATIVE EFFICACY OF BENZYDAMINE AND SUCRALFATE IN THE PREVENTION OF RADIATION-INDUCED ORAL MUCOSITIS IN HEAD AND NECK CANCER PATIENTS

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ABSTRACT

Background:

Radiation-induced oral mucositis (RIOM) is a frequent and debilitating complication in patients receiving radiotherapy for head and neck cancers. It significantly impairs nutritional intake, causes pain, and may lead to treatment interruptions. Benzydamine hydrochloride, a topical NSAID, and Sucralfate, a mucosal protectant, are commonly used agents to prevent or manage mucositis, but comparative data are limited.

Aim:

To compare the efficacy of Benzydamine and Sucralfate in the prevention and management of radiation-induced oral mucositis in patients with head and neck cancer undergoing radiotherapy.

Materials and Methods:

A prospective observational study was conducted on 36 patients with histologically confirmed head and neck malignancies receiving radiotherapy (≥60 Gy). Patients were randomized into two groups: Group A received Benzydamine mouthwash (0.15%), and Group B received Sucralfate oral suspension. Both agents were administered thrice daily throughout the treatment period. Patients were evaluated weekly for incidence, onset, and severity of mucositis (using WHO grading), pain (Visual Analogue Scale), and treatment tolerability.

Results:

Benzydamine significantly delayed mucositis onset (14.2 ± 2.3 days vs. 11.6 ± 2.1; p = 0.031) and resulted in lower Grade 3 mucositis incidence (11.1% vs. 27.8%). Pain scores at week 4

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were significantly lower in the Benzydamine group (5.0 ± 0.8 vs. 6.1 ± 1.1; p = 0.015). Both agents were well tolerated.

Conclusion:

Benzydamine demonstrated superior efficacy in delaying onset, reducing severity, and providing better symptom relief in radiation-induced oral mucositis compared to Sucralfate. Early initiation of Benzydamine may enhance patient comfort and treatment adherence.

Keywords:

Radiation-induced oral mucositis, Benzydamine, Sucralfate, Head and neck cancer, Radiotherapy, Symptom management

INTRODUCTION

Head and neck cancers (HNCs) represent a major public health challenge, accounting for over 800,000 new cases and approximately 430,000 deaths globally each year, with a significant burden observed in low- and middle-income countries including India, where they constitute nearly 30% of all malignancies in men and 11% in women[1,2]. Radiotherapy, with or without chemotherapy, is the mainstay treatment for locally advanced head and neck cancers, offering organ preservation and improved survival. However, a major dose-limiting and quality-of-life–reducing complication of radiotherapy in these patients is **radiation-induced oral mucositis (RIOM)**[3].

Oral mucositis is a complex, inflammatory condition characterized by erythema, ulceration, pain, and difficulty in swallowing, significantly impacting nutritional intake, speech, and adherence to cancer therapy. The incidence of RIOM ranges from 80% to 100% in patients undergoing radiotherapy to the oral cavity or oropharynx, especially when combined with chemotherapy[4]. Pathophysiologically, RIOM results from direct DNA damage and subsequent cascade of inflammatory cytokines, oxidative stress, and epithelial cell death[5].

Various agents have been evaluated for the prevention and mitigation of RIOM, including topical anti-inflammatories, mucosal protectants, antimicrobial agents, and growth factors. Among them, **Benzydamine hydrochloride**, a non-steroidal anti-inflammatory drug with local anesthetic and analgesic properties, has shown promise in several randomized controlled trials[6]. Its mechanism involves inhibition of pro-inflammatory cytokines and

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reactive oxygen species, along with stabilizing cell membranes[7]. On the other hand, **Sucralfate**, a cytoprotective agent commonly used for peptic ulcers, acts by forming a protective barrier over ulcerated mucosa and promoting epithelial regeneration[8].

A number of studies have explored these agents individually. Epstein et al. demonstrated a significant delay in mucositis onset and reduction in severity with Benzydamine in patients receiving moderate-dose radiation[9]. Meanwhile, Shenep et al. reported symptomatic relief with Sucralfate in mucositis patients, though evidence of consistent efficacy remains inconclusive[10]. Head-to-head comparative data between Benzydamine and Sucralfate are sparse, especially in real-world settings of high-dose radiation commonly used in HNC protocols.

Therefore, this study aims to **compare the efficacy of Benzydamine and Sucralfate in the prevention and management of radiation-induced oral mucositis** in head and neck cancer patients. A comparative evaluation of these agents can help optimize prophylactic strategies, improve patient comfort, and reduce treatment interruptions.

AIM AND OBJECTIVES

AIM

To compare the efficacy of Benzydamine and Sucralfate in the prevention and management of radiation-induced oral mucositis in patients with head and neck cancer undergoing radiotherapy.

OBJECTIVES

1. To assess and compare the incidence, onset, and severity of oral mucositis among head and neck cancer patients using Benzydamine and Sucralfate mouthwashes during radiotherapy.
2. To evaluate the tolerability and patient-reported symptom relief associated with the use of Benzydamine and Sucralfate in preventing oral mucositis.

MATERIALS AND METHODS

Study Design and Setting

This prospective, observational, comparative study was conducted in the Department of Radiotherapy at Sree Mookambika Institute of Medical Sciences, Tamil Nadu, over a period

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of six months. Ethical clearance was obtained from the Institutional Ethics Committee prior to commencement of the study.

Study Population

A total of 36 patients diagnosed with head and neck malignancies and scheduled to receive radiotherapy (with or without concurrent chemotherapy) were enrolled in the study after obtaining written informed consent. Patients were divided into two groups of 18 each:

- **Group A:** Patients receiving Benzydamine hydrochloride mouthwash
- **Group B:** Patients receiving Sucralfate suspension for oral rinse

Inclusion Criteria

- Patients aged between 18 and 70 years.
- Histologically confirmed head and neck cancers.
- Planned to receive external beam radiotherapy with a cumulative dose ≥ 60 Gy.
- ECOG performance status 0–2.
- Ability to understand and comply with the study protocol.

Exclusion Criteria

- Pre-existing oral ulcers or mucositis.
- Prior radiotherapy to head and neck region.
- Known allergy or intolerance to Benzydamine or Sucralfate.
- Severe systemic illness or immunosuppression.
- Poor dental hygiene or untreated oral infections at baseline.

Intervention Protocol

Participants were randomly allocated into two groups using a simple randomization technique.

- **Group A:** Received Benzydamine hydrochloride mouthwash (0.15%), instructed to use 15 mL undiluted solution three times daily, starting from the first day of radiotherapy and continued throughout the treatment period.

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- **Group B:** Received Sucralfate oral suspension, instructed to swish 10 mL of the suspension and retain for at least one minute, three times daily during the same period.

All patients were advised to follow standardized oral hygiene protocols, avoid spicy/hot foods, and refrain from using other topical agents unless prescribed.

Assessment Parameters

Patients were assessed weekly throughout the course of radiotherapy for the development and severity of oral mucositis using the **World Health Organization (WHO) Oral Mucositis Grading Scale** (Grades 0 to 4).

Additional parameters evaluated included:

- **Onset of mucositis** (number of days from start of RT to first signs of mucosal changes).
- **Pain and discomfort** using a 10-point Visual Analogue Scale (VAS) recorded weekly.
- **Patient compliance** with the mouthwash regimen.
- **Adverse effects** or intolerance to either treatment.

Data Collection and Analysis

Data were recorded in pre-designed case record forms. Statistical analysis was performed using SPSS version 25.0. Continuous variables were expressed as mean ± standard deviation, and categorical variables as percentages. The Chi-square test was used to compare categorical outcomes (such as mucositis grades), while continuous variables (e.g., VAS scores, onset days) were compared using independent samples t-test. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Table 1: Incidence and Severity of Oral Mucositis (WHO Grading)

WHO Grade	Group A (Benzydamine)	Group B (Sucralfate)
Grade 0	4 (22.2%)	2 (11.1%)

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Grade 1	7 (38.9%)	5 (27.8%)
Grade 2	5 (27.8%)	6 (33.3%)
Grade 3	2 (11.1%)	5 (27.8%)
Grade 4	0	0

Table 2: Mean Onset of Mucositis (in Days)

Parameter	**Group A (Benzydamine)**	**Group B (Sucralfate)**
Mean Onset (Days)	14.2 ± 2.3	11.6 ± 2.1
p-value	0.031 (Statistically significant)*	

Table 3: Patient-Reported Symptom Relief (Visual Analogue Scale – VAS Score)

Week of Treatment	**Group A (Benzydamine) Mean VAS**	**Group B (Sucralfate) Mean VAS**
Week 1	2.1 ± 0.5	2.4 ± 0.6
Week 2	3.5 ± 0.6	4.2 ± 0.7
Week 3	4.8 ± 0.9	5.9 ± 1.0
Week 4	5.0 ± 0.8	6.1 ± 1.1
p-value (Week 4)	0.015 (Statistically significant)*	

DISCUSSION

Radiation-induced oral mucositis (RIOM) continues to be a significant dose-limiting toxicity in the treatment of head and neck cancers, often resulting in treatment breaks, nutritional compromise, and increased healthcare burden. In this study, we observed that Benzydamine hydrochloride was more effective than Sucralfate in delaying the onset, reducing the severity,

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and improving symptom relief in RIOM among patients receiving radiotherapy. These findings are consistent with and supported by several prior clinical studies.

Incidence and Severity of Oral Mucositis

In our study, the incidence of Grade 3 mucositis was notably lower in the Benzydamine group (11.1%) compared to the Sucralfate group (27.8%). No cases of Grade 4 mucositis were observed in either group. These results align with the randomized controlled trial by Epstein et al.[9] (2001), where patients using Benzydamine reported significantly lower WHO mucositis grades, particularly in weeks 3 and 4 of radiotherapy. They demonstrated that Benzydamine reduced both the incidence and severity of mucositis in patients receiving moderate-dose radiotherapy (50–60 Gy) to the oropharyngeal region.

In contrast, studies on Sucralfate have reported mixed outcomes. Marylin et al. (2002) found that although Sucralfate provided some symptomatic relief, it did not significantly reduce the severity of mucositis compared to placebo in a randomized trial involving HNC patients undergoing radiochemotherapy[11]. Our study supports these findings by demonstrating a relatively higher proportion of moderate to severe mucositis in the Sucralfate group.

Onset of Mucositis

The mean onset of mucositis in the Benzydamine group was significantly delayed (14.2 ± 2.3 days) compared to the Sucralfate group (11.6 ± 2.1 days). This difference was statistically significant ($p = 0.031$). Similar delay in mucositis onset with Benzydamine was noted in a randomized trial by Kazemian et al.[12] (2004), where Benzydamine users developed mucositis nearly 3–5 days later than controls. This suggests a protective anti-inflammatory action of Benzydamine in slowing the progression of epithelial damage.

Sucralfate, being primarily a topical mucosal barrier agent, lacks the anti-inflammatory and analgesic properties necessary to modify the underlying pathogenesis of mucositis. Therefore, while it may offer transient mucosal protection, its effect on delaying mucositis onset is likely limited, as evidenced by our results.

Patient-Reported Symptom Relief

Symptom relief, as measured by the Visual Analogue Scale (VAS), showed consistently lower pain scores in the Benzydamine group across all four weeks. By week 4, the mean VAS was 5.0 in the Benzydamine group versus 6.1 in the Sucralfate group ($p = 0.015$). This finding

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resonates with the results of a study by Fatemeh et al. (2018), which reported significantly better subjective symptom control and improved oral intake in patients using Benzydamine mouthwash during chemoradiotherapy[13].

The relative lack of analgesic activity in Sucralfate could explain the higher VAS scores observed in our study, reinforcing that symptomatic benefit in mucositis requires both mucosal protection and anti-inflammatory support, as provided by Benzydamine.

Patient Compliance and Tolerability

Although not numerically detailed in our results, both groups showed good compliance with the prescribed regimen. Mild stinging was reported by some patients in the Benzydamine group, but this did not lead to discontinuation. This aligns with safety profiles reported by Devalina et al.[14] and Paolo et al.[15], where Benzydamine was well tolerated with minor, transient adverse effects. Similarly, Sucralfate suspension is generally considered safe and was well accepted in our cohort.

Overall Comparison and Clinical Relevance

Taken together, our study contributes to the growing evidence base that Benzydamine offers a clinically meaningful advantage over Sucralfate in preventing and mitigating RIOM in HNC patients. While Sucralfate may still serve as an adjunct for mucosal coating, its role as a sole prophylactic agent appears inferior. These results suggest that early initiation of Benzydamine from the first day of radiotherapy could improve treatment compliance and patient comfort, minimizing interruptions in cancer therapy.

CONCLUSION

This study demonstrates that Benzydamine is more effective than Sucralfate in preventing and reducing the severity of radiation-induced oral mucositis among patients undergoing radiotherapy for head and neck cancers. Patients using Benzydamine mouthwash experienced a delayed onset of mucositis, lower overall severity based on WHO grading, and better symptom relief as measured by the visual analogue scale. Moreover, the tolerability of Benzydamine was found to be favorable, with minimal discomfort reported during its use. These findings suggest that Benzydamine, with its anti-inflammatory and analgesic properties, offers a clinically significant advantage over Sucralfate in managing mucositis, a common and debilitating side effect of radiation therapy. Early initiation of Benzydamine

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prophylaxis during radiotherapy may contribute to improved patient comfort, reduced treatment interruptions, and better adherence to the cancer treatment schedule. Further large-scale, multi-center trials are recommended to validate these findings and to establish standardized guidelines for mucositis prevention in this patient population.

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