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UTILIZATION OF PRE- AND POST-COMPARATIVE ANALYSIS OF INTRA-LESIONAL DEXAMETHASONE COMBINED WITH HYALURONIDASE IN THE TREATMENT OF PATIENTS WITH ORAL SUBMUCOUS FIBROSIS: A CROSS-SECTIONAL STUDY

[1]Rahul Kumar, [2]Md Nayeemuddin, [3]Ashutosh Kumar*
[1]MS, Department of ENT, Shaheed Nirmal Mahto Medical College & Hospital, Dhanbad, Jharkhand, India.
[2]MS, Department of ENT, Phulo Jhano Medical College and Hospital, Dumka, Jharkhand, India.
[3]Professor, Department of ENT, Shaheed Nirmal Mahto Medical College & Hospital, Dhanbad, Jharkhand, India.

Abstract

Background

Oral Submucous Fibrosis (OSMF) is a chronic and potentially malignant disorder characterized by collagen deposition in the oral mucosa, primarily affecting the South Asian population. Despite its high prevalence and association with oral cancer, the pathophysiology of OSMF remains poorly understood, complicating effective treatment options.

Aim

To examine the efficacy of intra-lesional corticosteroid injections in alleviating symptoms and improving oral functionality in patients diagnosed with OSMF.

Methods

This clinic-observational study included patients diagnosed with OSMF. A total of 120 participants, aged 18 to 50 years, were administered intra-lesional injections of dexamethasone and hyaluronidase twice weekly for eight weeks. Clinical assessments, including mouth opening and burning sensation measured on a Visual Analogue Scale (VAS), were conducted tri-monthly. Statistical analysis was performed using SPSS to evaluate treatment efficacy.

Results

The study included 120 patients with OSMF, 68% (N = 82) were male, and 32% (N = 38) were female. The study revealed a significant improvement in mouth opening from 23.75 ± 2.54 mm pre-treatment to 27.50 ± 3.15 mm post-treatment ($p = 0.001$). Additionally, the VAS score for burning sensation decreased from 5.80 ± 1.30 to 2.90 ± 1.95 ($p = 0.001$), indicating effective symptom relief. These findings suggest that intra-lesional corticosteroid therapy significantly enhances oral mobility and reduces discomfort in patients with OSMF.

Conclusion

Intra-lesional corticosteroid therapy is an effective treatment for improving mouth opening and alleviating burning sensations in patients with OSMF. These results underscore the potential of corticosteroids in managing this precancerous condition and improving patients' quality of life.

Recommendations

The study recommends incorporating intra-lesional corticosteroid therapy as a primary treatment for OSMF due to its effectiveness in improving oral mobility and reducing discomfort. Additionally, further research is suggested to explore long-term outcomes and the benefits of combining this therapy with other treatment modalities.

***Keywords**: Oral Submucous Fibrosis, corticosteroids, intra-lesional therapy, mouth opening*
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***Corresponding Author:** Ashutosh Kumar*
***Email:** kumarashutosh1955@gmail.com*
Professor, Department of ENT, Shaheed Nirmal Mahto Medical College & Hospital, Dhanbad, Jharkhand, India.

Introduction

Oral Submucous Fibrosis (OSMF) is a progressive and long-standing disorder affecting the oral lining, marked by excessive buildup of dense fibrous collagen tissue in the submucosal layer, which can occasionally extend to the throat and esophagus. Clinically, OSMF manifests with signs like whitening and hardening of the oral tissues, restricted mouth opening (trismus), a burning sensation, reduced tongue movement, and impaired taste perception. This condition predominantly impacts the Indian population, with an estimated prevalence between 0.20% and 0.5%, especially in rural regions, where roughly 4 out of every 1,000 adults are affected. Notably, around 5 million young Indians are believed to be suffering from this pre-cancerous condition [1-3].

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As per the World Health Organization (WHO), OSMF has been classified as a potentially malignant disorder due to its connection with an enhanced predisposition to oral carcinoma [4]. The 2007 definition by Warnakulasuriya et al. highlighted the need for awareness of OSMF as a serious health concern, particularly in South Asian countries like Sri Lanka, India, Bhutan, Bangladesh, and Pakistan, as well as among South Asian immigrants worldwide [5-8]. This highlights the urgent need for effective management strategies to address the high prevalence and risks associated with this condition.

Despite extensive research, the etiopathogenesis of OSMF remains poorly understood, leading to confusion in management approaches. While various contributing factors have been studied, no consensus on a single pathophysiological mechanism has emerged, making the effective treatment of OSMF challenging. Given the promising therapeutic effects of corticosteroids observed in previous studies, our research aims to examine the efficacy of intra-lesional corticosteroid injections for the management of OSMF patients, contributing to the understanding and potential treatment options for this complex condition.

The study aims to examine the efficacy of intra-lesional corticosteroid injections in alleviating symptoms and improving oral functionality in patients diagnosed with OSMF.

Methodology

Study design

A clinic-observational cross-sectional study.

Study Setting

The study was conducted at Shaheed Nirmal Mahto Medical College & Hospital, Dhanbad, where patients attended the Department of ENT. This clinical setting provided a diverse patient population with varying degrees of Oral Submucous Fibrosis (OSMF), allowing for a comprehensive evaluation of intra-lesional corticosteroid treatment over a year-long period (August 2023 to August 2024). The hospital's established infrastructure and commitment to ethical research facilitated a structured approach to patient care and data collection.

Study Population

The study cohort encompassed OSMF patients aged between 18 and 50 years. Participants were recruited based on specific inclusion criteria to ensure that the findings were relevant and could be generalized to similar demographics. The chosen population provided a substantial sample size, enhancing the robustness of the study's outcomes.

Inclusion Criteria

Participants eligible for the study met the following criteria:

1. Individuals aged between 18 and 50 years.
2. Patients who consented to the study.
3. Individuals with a documented positive habit history, indicate potential risk factors associated with OSMF.

Exclusion Criteria

The exclusion criteria for this study included:

1. Patients with known allergic reactions to corticosteroids or other components of the treatment.
2. Individuals with systemic diseases, particularly those of an endocrine or metabolic nature, could affect treatment outcomes or patient safety.

Bias

To minimize potential sources of bias, several efforts were implemented. First, a standardized treatment protocol was followed for all participants, ensuring consistent administration of intra-lesional corticosteroid therapy. The study employed random selection criteria for participants, excluding those with systemic diseases or known allergies that could affect outcomes.

Reliability assessment

The examiner initially underwent a thorough training and calibration process within the Department of ENT before the start of the study. This process was supervised by a senior faculty member to ensure consistent examination techniques and accurate interpretations of clinical findings. The reliability of intra-examiner assessments was quantified using Kappa statistics, yielding a kappa value of 0.87, indicating a significant level of agreement in evaluations performed by the same examiner across multiple assessments.

Sample Selection

The sample size for the study was calculated using a power analysis with G* Power Software Version 3.0.1.0. Through this, a minimum sample of 120 participants was identified to be necessary to achieve a power of 0.90 with statistical significance. This sample size was deemed adequate to provide statistically significant results regarding the efficacy of intra-lesional corticosteroids in managing OSMF.

Methodology

Patient Demographics and Baseline Assessment

Demographic details and general health information of the participants were collected using a preformed questionnaire. This included data on age, gender, medical history, and specific oral symptoms related to OSMF. Baseline assessments were performed to establish a clear understanding of the patient's initial conditions. The medical history specifically focused on the patient's risk factors for Oral Submucous Fibrosis (OSMF), including

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habits such as tobacco chewing, areca nut consumption, smoking, and alcohol use. Additionally, the assessment covered any past treatments related to OSMF, systemic conditions (like diabetes or autoimmune diseases), and allergies to corticosteroids or other medications used in the treatment.

Treatment Administration

Participants received intra-lesional injections composed of 2 ml dexamethasone at a concentration of 4 mg/ml, along with 1500 IU of hyaluronidase, mixed with 0.5 ml of 2% lidocaine. These injections were administered biweekly over a period of eight weeks. The choice of dexamethasone and hyaluronidase was based on their known anti-inflammatory properties and potential to improve oral mucosal health.

Follow-up and Clinical Assessment

Clinical assessments of patients were conducted on a tri-monthly basis to monitor treatment responses. During each follow-up visit, the following parameters were evaluated:

- **Mouth Opening**: Measured using a ruler or caliper to determine any changes in oral mobility.
- **Burning Sensation**: Assessed using a Visual Analogue Scale (VAS), where participants rated their level of discomfort on a scale ranging from 0 (no pain) to 10 (worst possible pain). These ratings were systematically documented and compared at follow-up visits to gauge the treatment's effectiveness.

Data Analysis

The collected data were compiled in an Excel sheet and then analyzed using SPSS version 20 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics, including percentages, means, and standard deviations, were calculated to summarize the results. The student's t-test was used to compare baseline and follow-up measurements, with a 95% confidence interval and a significance threshold of $P \leq 0.05$. This statistical method ensured the reliability and accuracy of the findings.

Ethical considerations

The study protocol was approved by the Ethics Committee and written informed consent was received from all the participants.

Results

Demographic Profile of the Study Population

In this study, 120 patients diagnosed with OSMF participated. The demographic details are shown in Table 1. Of these, 68% (N = 82) were male, and 32% (N = 38) were female. The age distribution revealed that 12% (N = 14) were aged 18-27 years, 45% (N = 54) were between 28-37 years, 30% (N = 36) were aged 38-47 years, and 13% (N = 16) were over 47 years. Regarding education, 20% (N = 24) were literate, 50% (N = 60) had completed elementary school education, 22% (N = 26) had junior college-level education, and 8% (N = 10) were graduates. In terms of occupation, 12% (N = 14) were unemployed, 28% (N = 34) were skilled workers, and 60% (N = 72) were unskilled. The majority of participants resided in rural areas (55%, N = 66), followed by urban (25%, N = 30) and peri-urban (20%, N = 24) regions.

Table 1: Patient demographics of the study cohort

Variable	N (%)
Gender	
Male	82 (68%)
Female	38 (32%)
Age	
18 to 27 yrs	14 (12%)
28 to 37 yrs	54 (45%)
38 to 47 yrs	36 (30%)
> 48 yrs	16 (13%)
Education	
Literate	24 (20%)
Elementary school	60 (50%)
Junior College Education	26 (22%)
Advanced education	10 (8%)
Occupation	
Unemployed	14 (12%)
Skilled	34 (28%)
Unskilled	72 (60%)
Residence	
Rural	66 (55%)
Urban	30 (25%)
Peri-Urban	24 (20%)

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Mean Improvement in Mouth-Opening

The treatment showed a prominent improvement in mouth opening among the participants. As shown in Table 2, the mean mouth opening increased from 23.75 ± 2.54 mm pre-treatment to 27.50 ± 3.15 mm post-treatment, with a p-value of 0.001 ($p < 0.05$), indicating that intra-lesional corticosteroid therapy effectively enhanced oral mobility.

Table 2: Average Increase in Mouth Opening

Variable	Mouth Opening (mm)
Pre-treatment	23.75 ± 2.54
Post-treatment	27.50 ± 3.15
p-value	0.001 (Sig.)
Test applied	Paired sample t-test

Mean Improvement in VAS

Similarly, the assessment of burning sensation using the VAS demonstrated a significant reduction post-treatment. As illustrated in Table 3, the average score lowered from 5.80 ± 1.30 pre-treatment to 2.90 ± 1.95 post-treatment, with a p-value of 0.001. This result underscores the efficacy of the treatment in alleviating discomfort associated with OSMF.

Table 3: Average variation in VAS

Variable	VAS
Pre-treatment	5.80 ± 1.30
Post-treatment	2.90 ± 1.95
p-value	0.001 (Sig.)
Test applied	Paired sample t-test

Discussion

Around 45% of the participants in the present investigation were aged between 28 to 37 years, with an average age of 31.02 years. This age distribution aligns with findings from previous studies, such as [9], in whose study the average age of the patients was 29.12 years, and [10] who found most cases within the 21–40-year range. The high prevalence of OSMF in the younger population might be due to lifestyle changes, peer influence, stress, and the rising trend of addictive behaviors, such as the intake of areca nuts as well as tobacco products, which are common predisposing factors for OSMF.

The study also showed a marked male predominance, with 68% of the patients being male. This finding is consistent with previous research which also reported a higher prevalence of OSMF among men [11,12]. This gender disparity may be linked to cultural and societal factors, where males often have easier access to areca nut products, as well as lifestyle changes in younger men, including higher rates of smoking and tobacco chewing, which contribute to the higher incidence of OSMF among them [13].

Intralesional corticosteroid injections, particularly using dexamethasone and triamcinolone diacetate, are the most commonly employed treatment for OSMF, while other corticosteroids like methylprednisolone, betamethasone, and hydrocortisone are less frequently used [14]. In terms of treatment, this study used dexamethasone at a concentration of 4 mg/ml combined with 1500 IU of hyaluronidase and 2% lignocaine for intralesional injections. Significant improvements were noted in mouth opening and a substantial drop in the burning sensation, measured using the Visual Analogue Scale (VAS). These findings align with that of a study that reported significant symptom relief following similar treatment protocols [15]. In contrast, another research found no significant enhancement in mouth opening following the administration of steroids and hyaluronidase. This suggests that treatment results may differ based on variables such as the severity of the condition or the dosing protocol used [16].

Generalizability

The generalizability of the study findings is somewhat limited due to the specific population and setting in which the research was conducted. The study involved patients from a single medical institution in India, focusing on a South Asian population where Oral Submucous Fibrosis (OSMF) is highly prevalent. While the results may apply to similar populations with high rates of OSMF and similar risk factors (such as tobacco and areca nut use), they may not be directly transferable to populations in regions with lower OSMF prevalence or different etiological factors. Further studies in diverse settings would be needed to confirm the broader applicability of these findings.

Conclusions

The findings of this study indicate that corticosteroid treatment, when paired with hyaluronidase, is a beneficial approach for managing OSMF, particularly in enhancing

oral mobility and alleviating discomfort. This is crucial, given that OSMF is a progressive disorder associated with a significant risk of malignant transformation. Early intervention with corticosteroids may help in managing symptoms and potentially delay disease progression. Further research is needed to explore long-term outcomes and whether combining this treatment with other therapeutic modalities, such as antioxidants or physiotherapy, could enhance patient recovery and quality of life.

Limitations

The limitations of this study include a small sample population who were included in this study. Furthermore, the lack of a comparison group also poses a limitation for this study's findings.

Recommendation

The study recommends incorporating intra-lesional corticosteroid therapy as a primary treatment for Oral Submucous Fibrosis (OSMF) due to its effectiveness in improving oral mobility and reducing discomfort. Additionally, further research is suggested to explore long-term outcomes and the benefits of combining this therapy with other treatment modalities.

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List of abbreviations

OSMF: Oral Submucous Fibrosis
VAS: Visual Analogue Scale
WHO: World Health Organization
IU: International Units
MS: Master of Surgery
ENT: Ear, Nose, and Throat

Source of funding

No funding was received.

Conflict of interest

The authors have no conflicting interests to declare.

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