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Research Article

# Linking Diagnostic Accuracy with Effective Topical Chemotherapy in Ocular Surface Squamous Neoplasia Treatment

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## Abstract

**Objective:** To evaluate the effectiveness of an impression cytology-guided Mitomycin C treatment strategy in the management of Ocular Surface Squamous Neoplasia (OSSN) and to assess the outcomes of this management approach.

**Materials and Methods:** A prospective study was conducted at a tertiary healthcare centre, including 21 patients with cytologically diagnosed and histologically confirmed OSSN. Data collected included patient demographics, lesion characteristics, and treatment modalities, which encompassed both surgical excision and MMC therapy. The duration and dosage of MMC therapy were specifically tailored based on the findings from impression cytology. Following treatment, outcomes were meticulously analysed to assess the efficacy of this guided approach, including the resolution of OSSN, recurrence rates, and any associated adverse effects.

**Results:** Male predominance (61.9%) was observed among the patients, with a mean age of 43 years at presentation. Lesions were categorized by size and managed accordingly: lesions less than 5 mm underwent surgical excision followed by mitomycin C (MMC) in 38% of cases, while lesions between 5 - 10 mm were predominantly treated with MMC followed by surgical excision and additional MMC therapy (52.3%) and larger lesions exceeding 10 mm, involving critical areas like the canthus and fornices, received topical MMC 0.04% in pulse therapy in 9.52% of cases. By evaluating cellular morphology by impression cytology, MMC therapy was tailored more precisely. Post-treatment, 100% of patients experienced immediate symptomatic relief, with a recurrence rate of 9.52% in xeroderma patient with multisystem involvement. No significant MMC-related side effects were reported.

**Conclusion:** Mitomycin C demonstrated efficacy in treating OSSN, contributing to symptomatic relief and reducing recurrence rates without notable side effects. Tailored treatment strategies based on lesion size, location and cytological findings were effective in optimizing outcomes. Further research should explore multicentre trials to validate these findings and investigate emerging treatment modalities.

***Keywords:*** *Ocular Surface Squamous Neoplasia; Mitomycin C; Treatment Outcomes; Lesion Size; Recurrence*

## Abbreviations

OSSN: Ocular Surface Squamous Neoplasia; HPV Infection: Human Papillomavirus; MMC: Mitomycin C; UV: Ultraviolet Light

## Introduction

Ocular surface squamous neoplasia (OSSN) is a relatively common ocular surface tumour that arises from the conjunctival or corneal epithelium [1]. It typically presents as a slow-growing, raised, gelatinous or leukoplakic lesion on the eye's surface. OSSN is strongly associated with chronic exposure to ultraviolet light (UV), human papillomavirus (HPV) infection, immunosuppression, and cigarette

smoking [2,3]. Early detection and treatment are crucial to prevent potential vision loss or metastasis. Depending on the tumour's size, location, and extent of invasion, treatment options include surgical excision, cryotherapy, radiation therapy and topical chemotherapy with agents like mitomycin C (MMC), 5-fluorouracil or interferon α [4]. MMC is favoured for its potent cytotoxic effects and ability to penetrate deeper tissues, making it suitable for more aggressive lesions. MMC is utilized in treating OSSN through multiple modalities: topical application for surface lesions, intraoperative use to prevent recurrence post-surgery, and as an adjunct therapy alongside treatments like cryotherapy or radiation. Long-term follow-up is necessary due to the risk of recurrence and progression [5]. Impression cytology plays a critical role in managing OSSN by providing valuable diagnostic and therapeutic insights. This technique involves taking a cytological impression of the ocular surface to detect abnormal goblet cells, which indicate the presence of OSSN. During treatment with MMC, impression cytology guides the treatment strategy by assessing the extent of the lesion and ensuring complete resolution of the disease. It helps in planning MMC therapy more accurately, particularly in cases where the lesion is clinically free but still cytologically present. By utilizing impression cytology, clinicians can tailor MMC treatment to achieve complete removal of the disease and monitor for any residual or recurrent lesions effectively [6,7].Top of Form

## Materials and Methods

Total 21 eyes of 21 patients were included in the study having ocular surface squamous neoplasia (OSSN) and who visited department of ophthalmology, in a tertiary health care centre. A written informed consent was taken from all patients who qualified the inclusion and exclusion criteria.

### Inclusion criteria

- Patients with clinically diagnosed OSSN.
- Patient of any age group and sex.

### Exclusion criteria

- Patients with poor compliance.
- Patients not willing for investigations and not giving consent for management.

**Data collection**: Clinical data including patient demographics, presenting symptoms, lesion characteristics, histology, treatment history, and outcomes were collected prospectively in excel sheet and statistical analysis was done.

### Diagnostic evaluation

Patients clinically diagnosed with OSSN underwent impression cytology to assess goblet cell derangement and confirm cytological diagnosis. They were categorized into three groups based on lesion size, location, and morphology (flat or raised, gelatinous), each group receiving tailored treatment strategies. Small raised lesions, defined as those measuring less than 5 mm, were managed surgically with complete excision of the lesion by non-touch technique, which was supported with sub conjunctival cryotherapy beneath conjunctiva at edges with double thaw technique. Mitomycin C 0.04% was applied at the site after excision. Excised tissue was sent for histopathological examination to confirm the diagnosis aiding in treatment planning and prognosis.

Lesions that were medium-sized and raised, with poorly defined margins measuring between 5 to 10 mm, were first treated with MMC 0.04%. This involved administering MMC at a concentration of 0.04%, delivered four times daily in pulse therapy over one week, followed by a one-week treatment-free interval. Subsequently, surgical excision of the lesion was performed according to the previously outlined protocol.

Postoperatively, MMC 0.04% in pulse therapy was uniformly administered to all patients, regardless of margin status, to enhance treatment outcomes and reduce the risk of recurrence.

Large flat lesions, exceeding 10 mm in size and involving critical areas such as the canthus and fornices, were managed conservatively with topical MMC 0.04% in pulse therapy. Depending on the results of impression cytology, Mitomycin C (MMC) therapy was continued until cytology showed normal goblet cell morphology. Even after detecting no abnormalities in the impression cytology, it was repeated one month later to confirm complete resolution of the disease and to check for any signs of recurrence. Patients were then placed on a three-month follow-up schedule to monitor for any signs of recurrence [6,7].

## Results

Table 1 shows age and gender distribution in our study, in which male preponderance was seen (61.9%) while only minority (38%) females were seen. Majority patients belonged in the age group of 0 - 20 years (38%), 28.5% were seen in 60 - 80 years, minority belonged in the age group of 20 - 40 years (14.2%).

| Age Group | Male | Female | Total (%) |
|---|---|---|---|
| 0 - 20 years | 5 | 3 | 8 (38%) |
| 20 - 40 years | 2 | 1 | 3 (14.2%) |
| 40 - 60 years | 3 | 1 | 4 (19%) |
| 60 - 80 years | 3 | 3 | 6 (28.5%) |
| Total | 13 (61.9%) | 8 (38%) | 21 |

***Table 1:*** *Age and gender predilection in ocular surface squamous neoplasia.*

The aetiology in ocular surface squamous neoplasia observed was idiopathic in 47.6% while the remaining 42.8% had xeroderma pigmentosa and 9.52% were sero positive for human immunodeficiency virus, which is presented in table 2.

| Aetiology | Male | Female | Total |
|---|---|---|---|
| Xeroderma pigmentosa | 5 | 4 | 9 (42.8%) |
| HIV | 2 | 0 | 2 (9.52%) |
| Idiopathic | 6 | 4 | 10 (47.6%) |
| Total | 13 (61.9%) | 8 (38%) | 21 |

***Table 2:*** *Aetiology in ocular surface squamous neoplasia.*

Treatment strategies for ocular surface squamous neoplasia (OSSN) were tailored based on lesion size as depicted in table 3. Lesions less than 5 mm underwent surgical excision followed by MMC in 38% of cases (8 patients). Lesions between 5 - 10 mm were primarily treated with MMC first, followed by surgical excision and additional MMC therapy, accounting for 52.3% of cases (11 patients). Larger lesions exceeding 10 mm, involving areas like the canthus and fornices, received topical MMC 0.04% in pulse therapy in 9.52% of cases (2 patients).

| | Male | Female | Total |
|---|---|---|---|
| **Less than 5 mm** | 4 | 4 | 8 (38%) |
| Surgical excision followed by MMC | 4 | 4 | 8 |
| **Between 5 - 10 mm** | 8 | 3 | 11 (52.3%) |
| Topical mitomycin C 0.04% (MMC) only | 0 | 0 | 0 |
| MMC followed by surgical excision followed by MMC | 8 | 3 | 11 |
| **More than 10 mm (involving canthus and fornices)** | 1 | 1 | 2 (9.52%) |
| Topical mitomycin C 0.04% (MMC) in pulse therapy | 1 | 1 | 2 |
| Total | 13 | 8 | 21 |

***Table 3:*** *Size and management of ocular surface squamous neoplasia.*

Postoperatively, 100% of patients experienced immediate symptomatic relief from ocular surface squamous neoplasia (OSSN), while later 9.52% showed recurrence despite treatment with mitomycin C (MMC) 0.04%. No significant side effects related to MMC were reported, highlighting its favourable safety profile in this cohort.

| Post-op outcomes | Total (%) |
|---|---|
| Immediate Symptomatic relief | 20 (100%) |
| Recurrence | 2 (9.52%) |
| Side effects of mitomycin C | 0 (0%) |

***Table 4:*** *Post operative outcome in ocular surface squamous neoplasia.*

## Discussion

Ocular surface squamous neoplasia (OSSN) represents a significant ocular pathology characterized by its association with chronic UV exposure, HPV infection, and immunosuppression [2,3]. Our study sheds light on mitomycin C as a key treatment, showcasing its effectiveness in treating the condition with minimal side effects. This underscores MMC role in reducing OSSN recurrence and optimizing treatment outcomes, emphasizing its importance in clinical practice.

Our study affirms a higher prevalence of OSSN among male patients (61.9%) compared to female patients (38%), consistent with previous findings [5,8]. This gender imbalance is widely observed and likely influenced by diverse UV exposure patterns and genetic susceptibilities. Mean age at presentation was 43 years which is much lesser than that observed in other studies [9,10].

It was notable in our study that we conducted in tertiary care centre, a significant proportion (42.8%) of ocular surface squamous neoplasia (OSSN) cases were associated with xeroderma pigmentosa, while an additional 47.6% were categorized as idiopathic. This observation aligns with findings reported by Dirar, Qais S [11]. In contrast, other studies, such as those by De La Parra-Colin [12], highlight higher incidences of HPV-associated OSSN, particularly in immunocompromised individuals.

We served to utilize impression cytology as a diagnostic tool for assessing and monitoring OSSN, while subsequent histopathological examination also confirmed the diagnosis. Study by Chowdhury [1] have highlighted the utility of impression cytology in diagnosing OSSN, whereas other research, such as that by Mishra, Dilip Kumar [13], emphasizes the role of histopathology in confirming the diagnosis and guiding treatment decisions.

In our study, lesions with clear margins underwent excision, while flat lesions were monitored using impression cytology to track regression, recurrence, and follow-up. Recurrence was specifically noted in patients with xeroderma often associated with poor

compliance and multisystem involvement [14]. However, we observed no recurrences or adverse effects in patients without these risk factors, affirming the efficacy of our MMC approach as supported by previous studies [8]. Impression cytology served as a critical tool alongside MMC therapy, enabling real-time tracking of treatment effectiveness and disease recurrence. By using impression cytology to guide the continuation of MMC therapy, we were able to treat OSSN more effectively. Even when impression cytology showed normal goblet cell growth and MMC therapy was stopped, we repeated impression cytology to ensure complete resolution of the disease, a follow-up approach that has not been widely documented in other studies.

## Limitation of the Study

Limitations of our study include its single-centre setting and relatively small sample size, which may limit generalizability to broader populations. Future research efforts should focus on multicentre trials to validate our findings and explore emerging therapies such as immunomodulatory agents and targeted molecular therapies [15].

Impression cytology aids in monitoring treatment effectiveness and OSSN recurrence, while histopathology confirms the diagnosis. MMC demonstrates significant efficacy across lesion sizes and types, including cases of recurrence but requires rigorous monitoring.

## Conclusion

In conclusion, our study highlights the efficacy of mitomycin C (MMC) in managing ocular surface squamous neoplasia (OSSN), particularly in preventing recurrence across various aspects of treatment. Impression cytology played a vital role not only in diagnosing OSSN but also in guiding the application of MMC therapy based on cellular assessments. Importantly, we observed no MMC-induced side effects, highlighting its safety profile in our patient cohort. These findings emphasize the importance of tailored therapeutic approaches and rigorous follow-up in optimizing outcomes for patients with OSSN. Collaborative research efforts are crucial for refining treatment protocols and enhancing overall care in this challenging ocular condition.

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## Bibliography

1. Chowdhury Ravindra Kumar and Jayashree Dora. "Clinical profile of ocular surface squamous neoplasia a retrospective case series". *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)* 13.9 (2014): 53-55.

2. Shields Carol L., *et al*. "Conjunctival tumors: review of clinical features, risks, biomarkers, and outcomes—The 2017 J. Donald M. Gass Lecture". *Asia-Pacific Journal of Ophthalmology* 6.2 (2017): 109-120.

3. Mittal Ruchi., *et al*. "Ocular surface squamous neoplasia–Review of etio-pathogenesis and an update on clinico-pathological diagnosis". *Saudi Journal of Ophthalmology* 27.3 (2013): 177-186.

4. Sharma Manu. "Ocular surface squamous neoplasia: monotherapy with mitomycin C". *Journal of Clinical and Diagnostic Research* 14.6 (2020): ND01-ND02.

5. Menaka C., *et al*. "Role of mitomycin C in the management of ocular surface squamous neoplasia". *Kerala Journal of Ophthalmology* 32.2 (2020): 143-147.

6. Barros Jeison de Nadai., et al. "Impression cytology in the evaluation of ocular surface tumors". *Arquivos Brasileiros de Oftalmologia* 78.2 (2015): 126-132.

7. McKelvie Penelope A and Mark Daniell. "Impression cytology following mitomycin C therapy for ocular surface squamous neoplasia". *British Journal of Ophthalmology* 85.9 (2001): 1115-1119.

8. Puttaswamy Shashikala., *et al*. "Mitomycin C: An effective adjuvant in the management of ocular surface squamous neoplasia". *Clinical Cancer Investigation Journal* 2.4 (2013): 298-298.

9. Chen C., *et al*. "Mitomycin C as an adjunct in the treatment of localised ocular surface squamous neoplasia". *British Journal of Ophthalmology* 88.1 (2004): 17-18.

10. McKelvie PA and Daniell M. "Impression cytology following mitomycin C therapy for ocular surface squamous neoplasia". *British Journal of Ophthalmology* 85.9 (2001): 1115-1119.

11. Dirar Qais S., *et al*. "Effect of pegylated interferon and mitomycin C on ocular surface squamous neoplasia in xeroderma pigmentosum: a case series". *The American Journal of Case Reports* 21 (2020): e921301-1.

12. De La Parra-Colin Paola, *et al*. "Association of high-risk human papillomavirus with ocular surface squamous neoplasia: a case-control study in Mexico". *Salud Pública De México* 64.2 (2022): 209-217.

13. Mishra Dilip Kumar., *et al*. "Histopathological spectrum of ocular surface squamous neoplasia: A retrospective study of 776 lesions". *Indian Journal of Pathology and Microbiology* 65.1 (2022): 3-7.

14. Besley J., *et al*. "Risk factors for ocular surface squamous neoplasia recurrence after treatment with topical mitomycin C and interferon alpha-2b". *American Journal of Ophthalmology* 157.2 (2014): 287-293.e2.

15. Gurnani Bharat and Kirandeep Kaur. "Molecular and epigenetic mechanisms governing ocular surface squamous neoplasia: opportunities for diagnostics". *Expert Review of Molecular Diagnostics* 22 (2023): 1-15.

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