

## ORIGINAL RESEARCH

# To investigate the efficacy of topical mitomycin C as an adjuvant in the treatment of ocular surface squamous neoplasia

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### ABSTRACT

**Aim:** The purpose of this research is to investigate the efficacy of topical mitomycin C as an adjuvant in the treatment of ocular surface squamous neoplasia. **Material and methods:** Patients who had been given a diagnosis of OSSN and were above the age of 35 were considered for participation in the trial. A comprehensive history was obtained, including information on demographic characteristics, symptoms, their durations, and exposure to risk factors. Both the clinical exam and the cytological image were used to arrive at the conclusion that the patient had OSSN. **Results:** The OSSN reveals symptoms such as a sense of a foreign body in 6 participants (12%), a foreign body sensation plus a mass in 16 subjects (32%), and merely a mass in 22 subjects (with a high of 44%). Although damage and redness were seen in four of the patients (eight percent), just redness was observed in two of the subjects (four percent). The length of time that a person had OSSN was taken into consideration in the research. A greater number of individuals, or 19 (38%) of them, had OSSN for more than 8 months, whereas a smaller number of subjects, or 2 (4%), had OSSN for less than 3 weeks. 9 people were seen throughout the time of 3 weeks to 6 months, which corresponds to an 18% presence rate. In comparison, 4 subjects were seen for the duration of 3 months to 6 months, which corresponds to an 8% presence rate. There are many agents that can cause OSSN, but only four risk factors were considered for this study. Smoking was found to be a risk factor in 19 of the subjects (38 percent), while exposure to sunlight was found in 13 of the subjects (26 percent), and petroleum products were found in 7 of the subjects (14 percent). In 11 of the subjects, exposure to both sunlight and smoking was the risk factor that caused OSSN. **Conclusion:** The ophthalmology department often sees cases of OSSN, which is a dangerous kind of neoplastic illness. OSSN is rather prevalent. Wide excision is the conventional technique of therapy; nevertheless, this approach often results in a high risk of recurrence.

**Keywords:** Topical mitomycin, adjuvant, ocular surface squamous neoplasia

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### INTRODUCTION

The term "ocular surface squamous neoplasia" (OSSN) refers to a spectrum of benign, pre-malignant, and malignant unilateral epithelial lesions of the conjunctiva and cornea. These lesions are less progressing than others on the spectrum. Lee and Hirst were the ones who came up with the name "ocular surface squamous neoplasia" originally. The variables that make the condition worse include being exposed to UV radiation, having an infection caused by human papillomavirus type 16, having AIDS, having xeroderma pigmentosum, undergoing stem cell

treatment, having a genetic predisposition, smoking, and being immunosuppressed. Any change in the limbal stem cells might potentially lead to aberrant epithelial maturation and metaplasia, according to the notion put out by Lee and Hirst. This theory can be found here. Although while it may be found in other locations, it most often manifests itself in the interpalpebral fissure, specifically at the limbus. In most cases, symptoms such as eye discomfort or a tumor are not present until the late stages of maturity. In young adults, these lesions may also be detected, and they are associated with signs and symptoms such

as xeroderma pigmentosa and HIV infection [1-3]. The clinical manifestations of the lesions include gelatinous, leukoplakic, papilliform, nodular, or disseminated growths that may either be flat or raised [4,5]. There may be a feeder vessel present on occasion. The clinical examination is the most common method used to arrive at a diagnosis. Both an incisional and an excisional biopsy [6, 7] as well as a fine-needle aspiration biopsy need to be performed in order to get a clear diagnosis. Wide surgical excision and cryotherapy are the two components of the traditional treatment for OSSN. However, there are substantial recurring rates that may reach up to fifty percent [8,9]. In certain patients, several adverse effects have been seen, including the death of normal limbal stem cells and conjunctiva, which results in corneal neovascularization and the creation of symblepharon. Adjunctive treatments such as beta radiation [10], immunotherapy [11, 12], and topical chemotherapy [13, 14] have been utilized in an effort to reduce the number of recurrences of the disease and to avoid or minimize scarring as a result of several surgical procedures. Since 1994, various investigators [14-20] have shown that treating OSSN with topical mitomycin C MMC is effective in treating the condition. They found that the treatment of primary and recurrent OSSN with MMC in varying doses and for varying lengths of time had favorable effects for the patients. Because of the very high likelihood of recurrence, conservative medical therapy is quickly becoming more popular. The use of topical chemotherapy is the primary method of treatment. The agents mitomycin C (MMC), 5-fluorouracil, interferon alpha, and cidofovir are used on a consistent basis. MMC is typically selected over the rest of these options because it has the lowest overall cost and the fewest adverse effects [8]. It does this by blocking the creation of DNA, which in turn causes apoptosis and necrosis in the cells it affects. In addition to this, it inhibits the production of RNA and proteins inside the cell [9,10].

## MATERIAL AND METHODS

A prospective research including fifty participants was carried out. The research was given the go-ahead by the ethics committee, and everyone's permission was gathered before it began. Patients who had been given a diagnosis of OSSN and were above the age of 35 were considered for participation in the trial. A comprehensive history was obtained, including information on demographic characteristics, symptoms, their durations, and exposure to risk factors. Both the clinical exam and the cytological image were used to arrive at the conclusion that the patient had OSSN. Patients who had lesions that involved the sclera, those who had lesions that involved the intraocular or orbital structures, patients with any ocular disease, patients with any systemic illness such as HIV or any other immunocompromised conditions, and pregnant women were not allowed to

participate in the study. All of the participants in the research had been diagnosed with OSSN using a slit-lamp biomicroscope, and they all had OSSN that was less than five clock hours or fifteen millimeters in diameter. Visual acuity, refraction, the anterior segment, an evaluation of the shape, size, and extent to which the lesion is mobile, an evaluation of the anterior chamber reaction, involvement of the cornea and sclera, fluorescein staining, and 1% rose bengal staining were all part of the clinical examination of the subjects. This examination was performed using slit-lamp biomicroscopy. The correct procedure for treating OSSN is surgical excision of the lesion with a 3 mm margin of healthy tissue around it. This procedure should be performed without irrigation and with a single touch. After the excision of the tumor, the cut end of the conjunctiva under surface was subjected to cryotherapy for a duration of 25 seconds, while the cornea and limbus were treated for a duration of 15 seconds utilizing the double freeze thaw procedure. If the hole in the ocular surface was more than 25 mm by 25 mm, amniotic membrane grafting was performed. Otherwise, the ocular surface was allowed to mend on its own. After determining that the epithelial wound had been healed, all postoperative patients were given a topical solution of mitomycin C 0.04% four times a day for three to four cycles of alternating on and off weekly sessions. In circumstances when there was a big tumor or where surgery had to be postponed, preoperative topical mitomycin C was used. After the first phase of the treatment procedure, patients were contacted once per week for follow-up appointments, and this continued until therapy was completed. At the time of each appointment, in addition to the standard examination for recurrence of tumor and corneal modifications such as keratitis or erosions, a slit-lamp examination was conducted using rose bengal 1% and sodium fluorescein 1% drops. This was done in conjunction with the examination.

## RESULTS

The participants in the research ranged in age from 35 to 75 years old and all had OSSN. The study had 50 individuals. There are 8 subjects in the age group of 35-45 years, which accounts for 16% of all subjects; there are 27 subjects in the age group of 45-55 years (54%); there are 13 subjects in the age group of 55-65 years (26%); and the last subjects were 2 (4%). There are a total of 50 participants, 31 of which are male (62%) and 19 which are female (38%). (Table 1).

**Table 1: Gender and age distribution of the patients**

Gender	Number	%
Male	31	62
Female	19	38
Age		
35-45	8	16
45-55	27	54
55-65	13	26

Above 65	2	4
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The OSSN reveals symptoms such as a sense of a foreign body in 6 participants (12%), a foreign body sensation plus a mass in 16 subjects (32%), and merely a mass in 22 subjects (with a high of 44%). Although damage and redness were seen in four of the patients (eight percent), just redness was observed in two of the subjects (four percent). (Table 2).

**Table 2: Symptoms of OSSN**

Symptoms of OSSN	Number	%
Foreign body sensation+mass per eye	16	32
Mass per eye	22	44
Foreign body sensation	6	12
Redness	2	4
Injury+redness	4	8

The length of time that a person had OSSN was taken into consideration in the research. A greater number of individuals, or 19 (38%) of them, had OSSN for more than 8 months, whereas a smaller number of subjects, or 2 (4%), had OSSN for less than 3 weeks. 9 people were seen throughout the time of 3 weeks to 6 weeks, which corresponds to an 18% presence rate. In comparison, 4 subjects were seen for the duration of 3 months to 6 months, which corresponds to an 8% presence rate. (Table 3).

**Table 3: Duration of presentation of OSSN**

Duration of presentation of OSSN	Number	%
<3 weeks	2	4
3 weeks-<3 months	9	18
3 months-<6 months	4	8
6 months-<8 months	16	32
>8 months	19	38

There are many agents that can cause OSSN, but only four risk factors were considered for this study. Smoking was found to be a risk factor in 19 of the subjects (38 percent), while exposure to sunlight was found in 13 of the subjects (26 percent), and petroleum products were found in 7 of the subjects (14 percent). In 11 of the subjects, exposure to both sunlight and smoking was the risk factor that caused OSSN. (Table 4).

**Table 4: Risk factors in OSSN**

Risk factors in OSSN	Number	%
Sunlight	13	26
Sunlight+smoking	11	22
Smoking	19	38
Petroleum products	7	14

The post surgery marginal clearing was also taken into consideration in the research. At least one margin was seen in more individuals (23, or 46%), while margin clearance with dysplasia of two margins was observed in a smaller number of participants. (Table 5).

**Table 5: Marginal clearance post-surgery**

Margin showing dysplasia	Number	%
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Free margin	18	36
At least one margin	23	46
With two margin	9	18

**DISCUSSION**

Ocular surface squamous neoplasia (OSSN) in a broader terminology newly introduced in the field of ophthalmology that includes conjunctival malignancies which ranges from mild epithelial dysplasia to invasive squamous cell carcinoma (SCC). The frequent chemotherapy agent used for OSSN are 5 flurouracil, MMC, or interferon. Considering the cost factor and least adverse events, we preferred MMC as an adjuvant therapy along with surgical excision for assessing its efficacy in the treatment of OSSN. The study was done 50 subjects out of there were more number of male subjects as compared to female subjects which was similar to study done by other authors[21,22]. The risk factors affecting OSSN are sunlight, smoking, petroleum products ,almost all sunlight and smoking was the main risk factor of OSSN in our study which was similar to other studies[6,23]. The symptoms seen in OSSN are foreign body sensation, mass per eye, tumor, redness, injury, foreign body sensation and mass , Redness and injury were included in the study.Out of these maximum number of subjects included with symptoms were matching with the study compared with other reports published. The duration of OSSN was also included from less than 3 weeks to 8 months which was also similar to other studies comparing the number of subjects involved. Prabhasawat et al[20]. The Primary treatment for OSSN is surgical excision of lesion, as it is impossible to exclude invasive disease on clinical grounds or with impression cytology In spite the effort to excise the tumor with a wide healthy rim, only 18 cases (36%) had marginal clearance which was similar to study done by Shashikala Puttaswamy et al[24]. As considering various topical agents Mitomycin C, an alkylating agent which acts by inhibiting DNA synthesis and produces cell death by apoptosis and necrosis was preferred as adjunct in ocular surface squamous neoplasia[15]. As this drug has a privileged action for rapidly dividing cells, acts as a important antitumor agent and since 1994. A several groups have reported that use of MMC in the treatment of both primary and recurrent OSSN is very beneficial.

**CONCLUSION**

The ophthalmology department often sees cases of OSSN, which is a dangerous kind of neoplastic illness. OSSN is rather prevalent. Wide excision is the conventional technique of therapy; nevertheless, this approach often results in a high risk of recurrence. The use of MMC eye drops at a concentration of 0.04% has shown positive clinical outcomes, with no major adverse effects and a very low risk of recurrence in the condition being treated.

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