Review Article

The Role of Mitomycin C in the Treatment of Ocular Surface Squamous Neoplasia

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Abstract

Ocular surface tumors, arising from the squamous epithelium, melanocytes, and lymphocytic resident cells of the conjunctival stroma and cornea, present a challenge in ophthalmic oncology. Ocular surface squamous neoplasia (OSSN) encompasses a spectrum of epithelial squamous malignancies that range from mild to severe dysplasia to invasive squamous cell carcinoma. Traditionally, surgical excision has been the treatment of choice for OSSN, but Mitomycin C (MMC) has emerged as a valuable adjunctive treatment option, decreasing the recurrence rate of these tumors. This review provides an overview of the use of MMC in the management of OSSN, including dosing regimens, complications, and long-term outcomes.

Keywords: Mitomycin; Treatment; Ocular; Squamous Neoplasia.

Article Notes: Received: Dec. 03, 2022; Received in revised form: Jan. 04, 2023; Accepted: Jan. 28, 2023; Available Online: Apr. 02, 2023.

How to cite this article: Nassiri N, Shahriari M, Porkar Rezaeyeh A, Kavousnezhad S, Yadgari M. The Role of Mitomycin C in the Treatment of Ocular Surface Squamous Neoplasia. Journal of Ophthalmic and Optometric Sciences . 2023;7(2): 35-40.

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Introduction

Ocular surface tumors encompass a wide spectrum of neoplastic conditions affecting the conjunctiva and cornea [1]. These tumors originate from various cell types, including the squamous epithelium, melanocytes, and lymphocytic resident cells of the conjunctival stroma and cornea [1,2]. Despite advancements in surgical techniques, managing ocular surface tumors remains a challenge in ophthalmic oncology [3]. Traditionally, surgical excision has been the treatment of choice for ocular surface tumors [4]. However, the high risk of recurrence, infection, scarring, potential for extensive lesions, and the delicate nature of the ocular surface necessitate additional treatment modalities to achieve optimal outcomes [5].

Mitomycin C (MMC), an antineoplastic agent derived from Streptomyces bacteria, has gained attention as a valuable adjunctive therapy in the management of ocular surface tumors [6]. While MMC has been extensively studied and widely used in other fields of ophthalmic surgery, its application in ocular oncology has been relatively limited [7,8]. However, MMC has shown promise as a primary or adjuvant therapy for treatment of ocular surface neoplasia [9]. Studies have demonstrated its efficacy in various types of ocular surface tumors including ocular surface squamous neoplasia (OSSN), malignant melanoma, and recurrent conjunctival papillomatosis [10-13]. The utilization of MMC as an adjuvant therapy aims to enhance the effectiveness of primary surgical interventions and reduce the risk of tumor recurrence [12]. In addition to MMC, other adjuvant therapies, such as cryotherapy, β irradiation, interferon, and immunotherapy, have been explored for the management ocular surface tumors [14-18].

OSSN encompasses a spectrum of epithelial squamous malignancies that range from mild to severe dysplasia to invasive squamous cell carcinoma [19]. OSSN is the most common tumor of the ocular surface with an incidence of 0.02-3.5 cases per 100,000 worldwide [20]. The main treatment method for OSSN has been surgical excision, but it carries a high potential for recurrence and progression, necessitating additional treatment strategies [21].

In this review, we aim to provide an overview of the role of MMC in the treatment of OSSN. We will discuss its application as a primary or adjuvant therapy, dosing regimens, complications, and long-term outcomes.

The Use of MMS as the Primary Treatment for OSSN

The use of MMC as the primary treatment for OSSN offers advantages, including the simplicity of the procedure, and the avoidance of surgical complications such as limbal stem-cell deficiency and corneal scarring [22]. On the other hand, with this treatment method, tumor resolution is not immediate, and the number of follow-up visits required with medical treatment is higher compared to surgical treatment [22]. It should be noted that MMC as the primary treatment of OSSN has typically been used for less aggressive types, while surgical removal remains the treatment of choice for more aggressive forms of OSSN. The most important limitation of the use of MMC as the primary treatment for OSSN is the side effect profile, which may lead to the discontinuation of therapy [23]. Overall, topical MMC works well in eradicating OSSN, with high resolution and low recurrence rates [24, 25].

Dosing regimens

Different dosing regimens have been suggested for MMC when used as the primary

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treatment for OSSN. Gupta et al., [12] have used MMC 0.04 % four times a day on a week-on, week-off basis for two to three cycles, while Russell et al., [26] have suggested a regimen of 0.04 % MMC four times a day for 3 weeks on, 3 weeks off, 3 weeks on. Hirst [27] has recommended a regimen of 0.04 % MMC eye drops administered as 1 drop four times a day for 3 weeks, and Frucht-Pery et al., [28] have suggested MMC 0.02 % to 0.04 % four times a day for 7 to 28 days. Additionally, Ballalai et al., [29] have used 0.02 % MMC four times per day for 28 consecutive days.

Long-term outcomes

Long-term outcomes of MMC in the treatment of OSSN when used as a primary treatment have been promising. This treatment has been found to achieve tumor resolution in 76-100 % of cases, with a recurrence rate ranging from 0 % to 35 % [5].

The Use of MMS as the Adjuvant Therapy for Treatment of OSSN

Surgical procedures

The surgical procedure to treat OSSN includes tumor resection to remove the neoplastic tissue [4]. Adjuvant MMC is applied topically before, during, or after surgery to further improve treatment effectiveness and reduce the rate of recurrence [30].

Dosing regimens

The specific dosing and duration of MMC application as an adjuvant therapy for OSSN should be tailored to individual patients and the characteristics of the lesions, aiming to maximize treatment efficacy while minimizing the risk of complications [31]. The selection of an appropriate concentration and duration of MMC application depends on various factors, including the size, location, and invasiveness of the OSSN, as well as the surgeon's clinical judgment. Higher concentrations may be utilized for more severe or aggressive cases, while lower concentrations may be sufficient for milder cases.

The use of MMC before commencing surgery has been suggested to decrease tumor size, thereby minimizing the risks associated with surgery such as limbal stem cell failure. Singh et al., [32] used 0.04 % MMC eye drops four times a day in a 1-week-on, 1-week-off cycle for two cycles to reduce the size of the tumor before surgical resection. MMC can also be used intraoperatively or postoperatively in concentrations of 0.02 % or 0.04 % [5, 33]. Intraoperative MMC is applied to the bare sclera, followed by a thorough rinse with balanced salt solution [34]. In the postoperative period, MMC is used to prevent recurrence, commonly in cycles of 1 week on, 1 week off, dosed four times a day [35]. However, 1 week of MMC drops followed by a 3-week drug holiday, or 14 days of continuous MMC, have also been suggested [5].

Long-term outcomes

A recurrence rate of 0 % to 4.3 % when using MMC as adjuvant treatment for OSSN has been reported [25].

Complications

Although MMC has shown efficacy as an adjuvant therapy in the treatment of OSSN, its use is not without potential complications. Adverse effects associated with MMC include epithelial toxicity, scleral thinning, endothelial cell injury, corneal edema, cataract formation,

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and intraocular pressure elevation [36-40]. These complications highlight the importance of careful patient selection and close postoperative monitoring.

Conclusion

It seems that the use of MMC as a primary treatment or as an adjuvant to surgical therapy improves the outcomes of OSSN treatment. Further studies to evaluate the optimal dose and long-term outcomes are needed to enhance our understanding of its use in this application.

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Footnotes and Financial Disclosures

Conflict of interest:

The authors have no conflict of interest with the subject matter of the present manuscript.

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