

Conservative Treatment by Topical Mitomycin C as Primary and Sole Treatment Strategy for Localized Ocular Surface Squamous Neoplasia – A Success Story

Dr. Phoolchand Dhaka¹, Dr. Varsha Varshney^{2*}

¹Senior Specialist, Department of Ophthalmology, Churu Medical College & Associated Group of Hospitals, Churu, Rajasthan, India

²Senior resident, Department of Ophthalmology, Churu Medical College & Associated Group of Hospitals, Churu, Rajasthan, India

Original Research Article

*Corresponding author

Dr. Varsha Varshney

Article History

Received: 07.02.2018

Accepted: 21.02.2018

Published: 28.02.2018

DOI:

10.36347/sjams.2018.v06i02.042



Abstract: Our aim was to study the outcome of topical mitomycin C (MMC) used as sole treatment strategy for ocular surface squamous neoplasia (OSSN). This is a Prospective, non-comparative interventional case series of primary OSSN lesions of 15 patients treated in a single ophthalmology district hospital over a 5 year period. Study showed that 15 cases of OSSN received a treatment regimen of topical MMC 0.2% or 0.4%. Mean follow up of 24 months revealed no recurrences. So we concluded that MMC treatment alone can be used as a primary treatment strategy with very favourable results in both short term and long term follow up.

Keywords: Topical mitomycin c, ocular squamous neoplasia.

INTRODUCTION

Ocular surface squamous neoplasia (OSSN) is an umbrella term that encompasses dysplastic lesions involving the squamous epithelium of the conjunctiva or cornea [1]. Primary surgical excision remains the mainstay of treatment but the recurrence rate is high and various adjunctive therapies have been described [2]. Mitomycin C (MMC) has been used in the treatment of OSSN since 1994 [3], mainly for treatment of recurrent OSSN [4,5]. We present a series of 15 eyes with localised primary OSSN treated without any surgical intervention and adjunctive MMC. All the cases were treated primarily and solely with topical MMC eye drops reconstituted and given to the patients. The aim of this study is to report the success of conservative treatment and recurrence rate following treatment of primary OSSN using MMC as primary treatment strategy in a single ophthalmology centre over a 5 year period.

MATERIALS & METHODS

A single centre, prospective, non-comparative, interventional case series of 15 eyes in 15 patients with primary OSSN was carried out between January 2011 and February 2016.

Inclusion criteria included histologically confirmed noninvasive limbal OSSN (with associated corneal involvement) of less than 2 clock hours in extent. All treatment was carried out by a single surgeon. After confirmed histopathologic and clinical diagnosis, the patients were treated with reconstituted MMC eye drops in concentration of 0.02% in a dosing frequency of 4 times a day for 2 weeks. A total of maximum 3 cycles of 2 weeks ON and 1 week OFF the MMC therapy was carried out. The patients were examined during the therapy at weekly intervals and after complete clinical cure at 2 monthly intervals for at least 24 months. The primary outcome measure was clinical cure and recurrence of OSSN. Clinical cure was calculated based on the resolution in the size of the

lesion as seen by slit lamp under high magnification on regular follow ups.

RESULTS

There were 15 patients, five females and ten males, with 15 primary OSSN. The mean age was 60 (range 35–85) years. 3 patients received two courses because of allergy to MMC with redness, swelling, and significant itching, which developed late in the third course. All MMC allergy symptoms resolved rapidly following discontinuation of treatment. All patients have been followed up. The mean follow up period for the patients was 24 months (range 12– 50 months).

There was complete disappearance of the lesion and no evidence of clinical recurrence in any of these cases.

DISCUSSION

Ocular surface squamous neoplasia (OSSN) is a broad term encompassing conjunctival intraepithelial

neoplastic lesions (CIN) and invasive squamous cell carcinoma (SCC) of conjunctiva and cornea.(5) Our study represents the largest series to date of primary OSSN treated with topical MMC as primary treatment strategy. The authors believe MMC treatment alone is safe and effective therapy for local control as attested by the zero recurrence rate at a mean of 24 months. Primary excision has been the mainstay of treatment for OSSN [6]. The authors feel that superficial excision remains the important initial step in management as it is impossible to exclude invasive disease on clinical grounds or with impression cytology. Excision allows an immediate histopathological diagnosis, surgical debulking, and excludes life threatening invasive carcinoma [7]. The disadvantage of primary excision alone is the high recurrence rate which ranges from 15% to 52%.(8) Therefore, numerous adjunctive treatments have been described in an attempt to decrease the rate of recurrence and the efficacy of various adjunctive therapy have been debated. Intraoperative cryotherapy is commonly used as adjunctive therapy as it is known to decrease the recurrence rate by destruction of any residual tumour tissue beyond the horizontal or deep surgical margin of the wound [8]. Similarly Gupta et al. [9] concluded that MMC treatment following surgical excision appears to decrease the recurrence rate of localised CCIN and should be considered as adjuvant therapy in primary treatment. MMC should also be considered as adjuvant therapy in the treatment of localised recurrent disease. MMC may be used as sole therapy in more diffuse disease, but close ongoing follow-up is recommended in view of the significant risk of persistent or recurrent disease. Similarly Kalamkar C et al. [10] found that Diffuse OSSN in one eye was treated by monotherapy with topical MMC (0.04%) QID. Four cycles of topical MMC were given, each cycle consisting of 1 week on and 1 week off treatment. Follow-up at 1 year revealed no recurrences in OD. OS was also lesion free without any recurrence.

The use of topical chemotherapeutic agents, including Interferon- α 2b, mitomycin C, and 5-fluorouracil, has the advantage of treating the entire ocular surface and avoiding surgical complications such as positive margins, scarring, and limbal stem cell deficiency. Topical mitomycin C (MMC) has proven to be an efficacious treatment of OSSN. Mitomycin C is an antimetabolite that alkylates DNA and disrupts the production of RNA. Studies have reported its efficacy rate to range from 80% to 100%. MMC comes in either 0.02% or 0.04%. The lower concentration is usually prescribed continuously for a month; whereas, the higher concentration may be used for a week followed by 2 to 3 weeks off treatment. In our study, we noted 80% clinical resolution of the lesion after 2 cycles of therapy in 13 cases and 100% resolution by the end of 3 cycles. 2 cases showed little effect affect after 2 cycles but the lesion resolved completely at the end of 3 cycles.

Different protocols of topical MMC administration are being used, such as 0.02% topical MMC four-times daily to the affected eye for 2 weeks and repeated until the lesion regresses, or 0.04% four-times daily for 1 week with two to three cycles in alternate weeks. MMC can be stored at room temperature (22°C) for up to 1 week; if refrigerated (4°C), it can maintain 90% of its activity for longer. Stopping topical MMC or applying it in alternate weeks with the use of a topical steroid during the off-period is preferred due to increased patient comfort and compliance.

The disadvantages of MMC include ocular pain, possible limbal stem cell loss, and other ocular surface toxicity. Punctal plug occlusion is advised to decrease the risk of punctual stenosis.

The largest problem with MMC in our series was local allergy necessitating termination of treatment, as seen in 3 cases. None of our patients experienced significant corneal epitheliopathy and this may be attributed to the 2 week on, 1 week off regimen which prevents damage to more slowly dividing epithelial cells and limbal stem cells, allowing them to repair their DNA. We believe that allowing time for complete epithelial healing before application of MMC is important in avoiding the more serious complications such as scleral ulceration, uveitis, cataract, and glaucoma. We noted no systemic side effects as a result of topical MMC treatment.

CONCLUSION

In conclusion our study demonstrates that MMC treatment alone can be used as a primary treatment strategy with very favourable results in both short term and long term follow up.

REFERENCES

1. Lee GA, Hirst LW. Incidence of ocular surface epithelial dysplasia in metropolitan Brisbane: a 10-year survey. *Archives of Ophthalmology*. 1992 Apr 1;110(4):525-7.
2. Lee GA, Hirst LW. Ocular surface squamous neoplasia. *Survey of ophthalmology*. 1995 May 1;39(6):429-50.
3. Majmudar PA, Epstein RJ. Antimetabolites in ocular surface neoplasia. *Current opinion in ophthalmology*. 1998 Aug;9(4):35-9.
4. Daniell M, Maini R, Tole D. Use of mitomycin C in the treatment of corneal conjunctival intraepithelial neoplasia. *Clinical & experimental ophthalmology*. 2002 Feb 1;30(2):94-8.
5. Mittal R, Rath S, Vemuganti GK. Ocular surface squamous neoplasia—Review of etio-pathogenesis and an update on clinico-pathological diagnosis. *Saudi Journal of Ophthalmology*. 2013 Jul 1;27(3):177-86.
6. Khokhar S, Soni A, SinghSethi H, Sudan R, Sony P, Pangtey MS. Combined surgery, cryotherapy,

- and mitomycin-C for recurrent ocular surface squamous neoplasia. *Cornea*. 2002 Mar 1;21(2):189-91.
7. Vann RR, Karp CL. Perilesional and topical interferon alfa-2b for conjunctival and corneal neoplasia. *Ophthalmology*. 1999; 106(1):91-7.
 8. Kaines A, Malhotra R, Selva D. Conjunctival squamous cell carcinoma with perineural invasion. *Arch Ophthalmol*. 2005 May-Jun;36(3):249-51.
 9. Gupta A, Muecke J. Treatment of ocular surface squamous neoplasia with Mitomycin C. *British Journal of Ophthalmology*. 2010; 94(5):555-8.
 10. Kalamkar C, Radke N, Mukherjee A, Radke S. Topical Mitomycin-C Chemotherapy in Ocular Surface Squamous Neoplasia. *Journal of clinical and diagnostic research: JCDR*. 2016 Sep; 10(9):NJ01.