

## EFFICACY OF TOPICAL MITOMYCIN-C EYE DROPS IN THE TREATMENT OF NODULAR EPISCLERITIS

### Ophthalmology

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### ABSTRACT

Nodular episcleritis is a common ocular disorder affecting middle aged women more than men. Various treatment modalities have been suggested for this malady. But none of them are effective since the recurrence rate is very high. Topical steroids are the only drugs responsible for obviating the symptoms. However, long term use of steroids is contraindicated due to its various complications. We have studied these cases with topical Mitomycin-C eye drops with excellent results, as discussed in this article.

### KEYWORDS

Topical Mitomycin-C eye drops, nodular episcleritis

#### Introduction:

Nodular episcleritis is a severe inflammatory disorder that involves the opaque collagenous outer coat of the eye, called the episclera, which lies between the conjunctiva and sclera. This disease is often idiopathic, but can also be caused due to bacterial, fungal and parasitic agents. It occurs more commonly in females than in males, with a peak incidence in the 4<sup>th</sup> and 6<sup>th</sup> decades, and is bilateral in 50% of the cases. There may be very severe pain, and it is often associated with photophobia and lacrimation.

The complications of nodular episcleritis are mainly due to corneal changes such as:

- Deep keratitis
- Keratolysis which can cause severe diminution of vision

Other complications include uveitis, scleral thinning, optic nerve inflammation and glaucoma.

#### Side effects of the presently used drugs in the treatment of nodular episcleritis:

Non-steroidal anti-inflammatory agents: Itching, burning, foreign body sensation and other dry eye related symptoms. There are more chances for recurrence. They may also cause corneal epithelial failure.

**Steroids:** A daily dose of around 10mg of prednisolone is regarded as the Cushing threshold.

The systemic side effects of steroids include osteoporosis, pancreatitis, peptic ulcers, Cushing's syndrome, myopathy, impaired collagen formation, delay in wound healing. Periocular dermatitis and diffuse retinal pigment epitheliopathy are rare complications seen with systemic steroid therapy.

There are also several ocular side effects of steroids such as glaucoma, cataract and pseudotumour cerebri. On topical application, steroids can give rise to changes in the cornea, decrease in the collagen synthesis, delayed wound healing, increased vulnerability to ocular infections such as herpes, fungal infections, toxoplasmosis, recurrent HSV keratitis. Other complications include ptosis, and mydriasis.

The aim of this study was to determine the most efficient and least toxic mode of treatment in cases of nodular episcleritis, by maintaining the patient's quality of vision as well as by achieving complete resolution from its progression and recurrence.

Immunosuppressive therapy is considered to be the third choice of treatment, when topical non-steroidal anti-inflammatory drugs as well as topical and systemic steroids fail to control the inflammation or in those who develop complications, due to high maintenance dose of steroids. In cases with very severe nodular episcleritis or in nodular episcleritis associated with various collagen vascular disorders, such as rheumatoid arthritis, SLE, polyarteritis nodosa, Wegener's granulomatosis and relapsing polychondritis, immunosuppressive

therapy can be beneficial.

#### Mitomycin-C 0.02% eye drops:

Mitomycin-C is an anti-neoplastic antibiotic produced by the growth of the organism *Streptococcus caseiposus*, with a potency of not less than 970 micrograms/mg. It is an alkylating antibiotic that acts on all phases of the cell cycle and inhibits DNA synthesis. It is absorbed inconsistently from the gastrointestinal tract on systemic administration. Although it has a wide distribution throughout the body, it is not detected in the brain. Interaction occurs by metabolism or by chemical conjugation.

#### Materials and Methods:

50 patients diagnosed to have nodular episcleritis in our OPD were selected for the study. The patients were grouped in to 2 groups – group A and group B. Patients who were treated only with topical steroids were grouped under group A, whereas group B had patients who were treated with topical Mitomycin-C eye drops.

#### Inclusion criteria:

Patients above the age of 18 years, who were diagnosed to have nodular episcleritis:

- Nodular episcleritis in whom the benefits of the treatment need to be weighed against the risk of developing ocular complications.
- Recurrent cases.
- Nodular episcleritis associated with collagen vascular disease.
- Not responding to non-steroidal anti-inflammatory agents.

#### Exclusion criteria:

- Toxicity to topical Mitomycin-C such as iridocyclitis, cataract, glaucoma and scleral ulceration.
- Patients with myelosuppressive diseases.
- Patients having impaired renal function.
- Patients with delayed epithelial healing.
- Patients with coagulation disorders.
- Pregnant and lactating females.

Depending on the severity of nodular episcleritis, Mitomycin-C 0.02% and 0.04% eye drops were instilled 3 to 4 times a day in Group B patients. As per Table 1, 35 of the patients were found to be females, majority of them belonging to the 40-50 years age group. Figure 1 shows a prevalence of females in all age groups.

With respect to the etiology, as seen in Figure 2, 80% of the patients belonged to the idiopathic group and only 20% had associated collagen disorders.

Baseline assessment of the patients was carried out in the OPD, which included detailed history taking and ocular examination. Recording of visual acuity, slit-lamp examination and fundoscopy was performed. Blood pressure and heart rate were regularly monitored and the

patients underwent monthly blood tests, including WBC counts.

| Table 1: Age and sex distribution |                 |        |                 |        |
|-----------------------------------|-----------------|--------|-----------------|--------|
| Age group in years                | Group A         |        | Group B         |        |
|                                   | No. of patients |        | No. of patients |        |
|                                   | Male            | Female | Male            | Female |
| 20-30                             | -               | 1      | 2               | 1      |
| 30-40                             | 3               | 3      | 1               | 5      |
| 40-50                             | 3               | 9      | 5               | 11     |
| Above 50                          | -               | 2      | 1               | 3      |

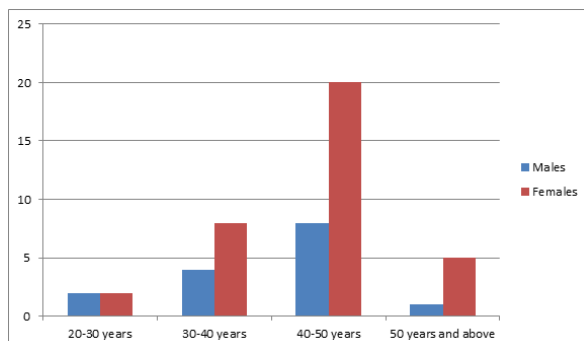


Figure 1: Age and sex distribution of patients with nodular episcleritis

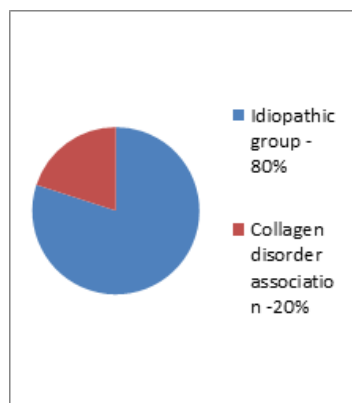


Figure 2: Etiological classification of patients with nodular episcleritis

### Results:

The patients were followed up every week. In group A, there was incomplete resolution of the scleral inflammation seen at the end of the first month. Group A also showed a recurrence of the attacks of episcleritis thereafter. Marked improvement was observed in the first week of treatment in group B. All patients tolerated the instillation of topical Mitomycin-C eye drops well. There was a decrease in redness, pain as well as sclera oedema. A complete resolution of the scleral inflammation was observed in about 16 patients at the end of the second month, and in about 13 patients at the end of the third month.

### Discussion:

Mitomycin-C is an antineoplastic antibiotic produced by the organism *Streptomyces caedepitosis*. [1] In selected patients, it is effective in improving the results of glaucoma filtering surgery, when used as an adjunct as it helps in minimizing scar tissue formation. [2] One of the most common ocular side effects seen with the use of Mitomycin-C is the development of chronic hypotony, with or without maculopathy, which may lead to irreversible loss of vision. [3] Mitomycin-C has also been used topically in pterygium excision surgery for application over the surgical site, or even as postoperative eye drops. [4] The ideal concentration to be used for topical use is uncertain. 0.04% Mitomycin-C eye drops have been used. [5] However, a 0.02% solution may show efficacy as well as better tolerance. [6] According to EG Kemp et al, chemotherapy with Mitomycin-C topically and intra-operatively has many advantages as compared to limited excision alone, especially in cases with diffuse and recurrent ocular lesions. Mitomycin-C has been used in ophthalmological practice for both its

cytotoxic as well as antifibrotic actions. It has been shown to have an effect on the subconjunctival fibroblasts. [7] Serious complications reported with the topical use of Mitomycin-C include sclera thinning, cataract, iridocyclitis and glaucoma (Yamannouchi U et al). It has also been reported to be used as a wound modulator after excimer laser refractive surgery (Talamo JH et al).

### Conclusion:

Instillation of topical Mitomycin-C eye drops is advantageous over other modes of therapy such as NSAIDs, which show a slow response and high recurrence rate, and steroids, which also show recurrence, development of resistance, intolerance and several ocular and systemic side effects.

Topical Mitomycin-C eye drops were seen to be well tolerated. They had an extremely high success rate and almost no side effects when used for a short duration, as in case of our patients. The antifibrotic action of topical Mitomycin-C lasts for a fortnight even after discontinuing the drug.

This is one of the original studies that has evaluated the management of nodular episcleritis using topical Mitomycin-C eye drops. Literature shows only few published data of similar nature at present. The use of Mitomycin-C for various ocular conditions such as recurrent pterygium and in glaucoma filtering surgery for its antifibrotic action stimulated this study on the use of the same drug in the treatment of nodular episcleritis.

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