The efficacy of using intraoperative compared with postoperative topical 0.04% Mitomycin-C drops to the recurrence of Pterygium

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ABSTRACT

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Background: The major problem in the treatment of pterygium is to prevent recurrences after surgical excision. To prevent the recurrence, both excision and recurrence. waterproof dress and administration of mitomycin-C instillation had been used. However, no slice treatment has been universally effective yet.

Objective: The purpose of this study is to evaluate the safety and efficacy of two different methods of 0.04% Mitomycin-C application, as adjunctive chemomotherapy in the recurrence of pterygium.

Methods: The research had been conducted in the Dr. Sardjito Central Hospital, Wates Clinical Hospital, Gresik Central Hospital, and Purwokerto Aisah Hospital from January 1995 to December 1998. Eighty-eight patients underwent pterygium excision were involved in this study, and divided into two groups. Group I or intraoperative 0.04% MMC group of 44 cases receiving 0.04% MMC drops applied in the bare sclera for 4 minutes intraoperatively. Group II or postoperative group of 44 cases receiving 0.04% MMC one drop on the day after excision once daily during the first postoperative week and continued with a drop of one drop 3 times a day during the second postoperative week. Observations were done daily during the first postoperative week, and monthly up to 6 months. Observations were done including the symptoms of recurrence and side effects of the treatment. The data were analyzed using the Student’s t-test and chi square technique.

Results: In the intraoperative group, 6 cases (13.6%) recurred, 2 cases of superficial punctate keratitis. In the postoperative group, 7 cases (16.3%), and 7 cases of superficial punctate keratitis. There was no statistical difference in the rates of recurrence (α = 0.05, p > 0.05). Most of the cases of pain, tearing and lid edema occurred in the group in post-operative. No other complication was observed in the course of the study.

Conclusions: A single drop intraoperative application of MMC is a simple, economic, effective alternative adjunctive treatment for pterygium.

Key words: Intraoperative Mitomycin-C – pterygium excision - recurrence

ABSTRAK

Suhardjo - Daya guna penggunaan mitomisin C 0.04% teras mata intra-operasi dibandingkan pascaoperasi terhadap kekambuhan pterygium

Latar belakang penelitian: Masalah utama pada pengobatan pterygium adalah nusacah kekambuhan pasca pembuangan. Tetapi bermabah cara guna AGC (aqua gelatins) dan administrasi mitomisin C untuk menghindari timbulnya neovaskularisasi dan kekambuhan pterygium, namun demikan belum ditemukan bencar cara pencegahan yang efektif.

Metode penelitian: Pembahasan ini dibintangi terhadap daya guna dua cara penggunaan mitomisin-C 0.04% dilakukan kelompok I atau intraoperasi dan kelompok II atau pascaoperasi.

INTRODUCTION

Pterygium constitutes the third most common eye disease in Indonesia. The result of surgery for pterygium are reasonably good, but recurrences are frequent, ranging from 0-69.4%1,2. Repeated surgical procedures often worsen the situation, as loss of the conjunctival tissue and scarring can result in obliteration of the fornixes. To prevent the neovascularization and recurrence, many researchers used Streptomyces calpitsatus, that may inhibit the synthesis of cellular DNA, RNA and protein. Variable dose of MMC instillation has been used. Mori et al reported the MMC instillation three times daily for 2 weeks and the recurrence rate of 13%, but severe scleral damage and scleral oedema were reported as complication of pterygium excision and using post operative MMC drops by some ophthalmologist in Yogyakarta still occurred. On the other hand, intra-operative MMC as adjunct chemotherapy with pterygium excision had shown good result.3,7 The problems of the study is : which one among those methods has lower recurrence rate and more safety.

The purpose of this study is to evaluate safety and efficacy of two different regimen of MMC application as adjunctive chemotherapy to the recurrence of pterygium. These knowledge will render a more appropriate treatment, a better cure rate, and less complication.

MATERIALS AND METHODS

Patients with pterygium attending the ophthalmic outpatient clinic of Dr Sardjito Central Hospital, Yogyakarta, were included in the study. 22 patients received MMC 91% 1x weekly for 1 month and 22 patients received MMC 91% 3x weekly for 1 month. Results were compared using Student t test. A significant difference was declared when the p-value was less than 0.05.

RESULTS

A significant difference was found between the two groups in terms of recurrence rate (25% vs 77%, p<0.05). The recurrence rate was lower in the group that received MMC 91% 1x weekly compared to the group that received MMC 91% 3x weekly.
in the second week. The patients group II receiving 0.04% MMC. One drop every day together with topical steroid-antibiotic eye ointment in the first week, and 3 times one drop together steroid-antibiotic drops in the second week. Observation was done daily for one week, weekly for one month, and monthly up to 6 months. At each visit, a full ophthalmologic examination was performed and any ocular tissue changes was observed. Recurrences were defined as any conjunctiva tissue starting to pass the limbus.

The results are expressed as mean, and frequency. The data were analyzed using the Student's t test and chi square. The minimum level of significance was considered as \( p < 0.05 \).

RESULTS

The patients age range between 27-72 years in group I, and 17-60 years in group II. Each group consisting of 29 females and 15 males, and group II consisting of 27 females and 17 males. All patients live in rural territories, and almost all patients work as farmer with daily sunlight exposure.

The mean age of group I was 35.69 ± 4.70 years and 52.93 ± 8.84 years. In the group II, the mean age was 31.05 ± 6.10 years and 30.86 ± 6.55 years. Statistically, there were no difference in age and sex between group I and group II (TABLE 1).

Indonesia is a tropical area which encircles the earth this extends from 37 degrees north to 37 degrees south of the equator. Pterygium in Indonesia is considered to be the manifestation of chronic irritation by solar radiation, repeated micro trauma and abnormality of tear film. Many patients who had thick vascular pterygia (inflamed type) and the other patients had thin membranous pterygia. More than one half patients were 40 years old and more had thin membranous pterygia. By chi square test analysis, there was no difference in recurrence rate between the young group (< 40 years old) and the old group (≥ 40 years old) in both groups (TABLE 2). All pterygium that occurred (16 cases) during the follow-up period were retreated with excision and then received postoperative MMC drops four times daily for 2 weeks.

Neovascularization, granulations and recurrence occurred in 6 patients (13.67%) in group I and 7 patients (15.91%) in group II. However, these differences were not statistically significant (\( x^2 = 0.0902, p > 0.05 \)). No recurrence found in patients of more than 50 years old. All pterygia that occurred (11 cases) during the follow up period were retreated with excision and then received intra-operative and postoperative MMC 0.04% for 2 weeks.

The postoperative complications were relatively comparable between two groups (TABLE 3). In the patients treated intrasoperatively, there were 2 cases of superficial punctate keratitis, 3

<table>
<thead>
<tr>
<th>TABLE 1. - Demographic data all patients</th>
<th>Data</th>
<th>Group I</th>
<th>Group II</th>
<th>Statistical analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>26-70 Years</td>
<td>17-60 Years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean age (&lt; 40 years)</td>
<td>35.69 ± 4.70</td>
<td>31.05 ± 6.10 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean age (≥ 40 years)</td>
<td>52.93 ± 8.84</td>
<td>50.86 ± 6.55 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>male</td>
<td>15</td>
<td>17</td>
<td>( x^2 = 0.18 * )</td>
</tr>
<tr>
<td></td>
<td>female</td>
<td>29</td>
<td>27</td>
<td>( x^2 = 0.30 * )</td>
</tr>
</tbody>
</table>

\( p > 0.05 \)

<table>
<thead>
<tr>
<th>TABLE 2 - Age group and recurrence rate after 6-months follow up</th>
<th>Group</th>
<th>Number of cases</th>
<th>Recurrent Cases</th>
<th>Recurrent rate</th>
<th>Statistical analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (Postoperative)</td>
<td>40 years old</td>
<td>14</td>
<td>3</td>
<td>21.43%</td>
<td>( x^2 = 1.051 * )</td>
</tr>
<tr>
<td></td>
<td>≥ 40 years old</td>
<td>36</td>
<td>3</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td>II (Postoperative)</td>
<td>≤ 40 years old</td>
<td>21</td>
<td>2</td>
<td>9.53%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥ 40 years old</td>
<td>23</td>
<td>5</td>
<td>21.74%</td>
<td>( x^2 = 1.223 * )</td>
</tr>
</tbody>
</table>

\( p > 0.05 \)
cases of pain, 3 cases of tearing and 2 cases of lid edema. In the patients group II, only 3 cases of superficial punctate keratitis occurred.

<table>
<thead>
<tr>
<th>Side effects</th>
<th>Group I</th>
<th>Group II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial punctate Keratitis</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Pain</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Tearing</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Lid edema</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

Side effects occurred in group I were pain, tearing, lid edema, infection, ulceration, uveitis, glaucoma and necrosis of the sclera did not occur. Slight photophobia which disappeared after 7 days after application in almost all patients. No systemic complications were experienced.

DISCUSSION

Pterygium is a degenerative corneal limbal process characterized by exuberant fibrous tissue proliferation of unknown etiology. It is a common condition in Indonesia. Hot, wet and dry climates and ultra violet radiation have been implicated as major predisposing factors at primary pterygium occurrence. Pterygium is composed in part of newly by synthesized elastic fibers that is presumably elaborated by actinically damaged fibroblasts of the substantia propria. In the literature, different rates of recurrence were reported by many authors. Rabie reported that the recurrence rate of laser surgery for pterygium was 0%, but Mokhe 17.78 - 69.44%. Many research workers reported various doses of MMC to reduce the recurrence rate. Siti Tjahjono 9 using 0.1 mg/ml MMC intraoperatively as adjunct chemotherapy with pterygium excision found 10.7% recurrence rate. Helal et al7 using the same concentration found 5.57% recurrence rate. Many modulation of adjunctive treatments with variable success rates have been developed, but no single treatment has been universally effective. An important principle in the prevention of recurrence is to stop the new vessel formation in the basal episceral surface. Rapid epithelialization also helps to diminish the formation of granulation tissue. MMC inhibits DNA synthesis, this prevents cell division and diminishing cell viability. Its greatest antiproliferative effect is on the cells that show the highest rate of mitosis. MMC usage with pterygium excision retarded the growth of granulation tissue by its antiproliferative effect. There was no statistical difference in the rates of recurrence or postoperative complications between the two groups. The intraoperative application of MMC has the advantages of not being influenced by patient compliance, requiring fewer post operative medications, and a lesser chance of developing a cumulative dose of MMC.

Singh et al11 reported ocular pain, photophobia, tearing, and foreign body sensation in the first to second week postoperative. They were marked when they used a 1 mg/ml concentration rather than 0.4 mg/ml concentration of MMC drop. Some of these symptoms remained as long as 6 to 8 weeks postoperative in some patients especially in inflamed type.

Rubinfield et al12 described a series of ten patients who experienced serious vision – threatening complications associated with the use of MMC after pterygium surgery. These included severe glaucoma, corneal edema, corneal perforation, corneal opacity, iris, sudden onset of mature cataract, scleral calcification, incapacitating photophobia, and pain. The MMC concentration, the surgical technique, the use of too much cautery or the presence of underlying ocular or systemic disease may contribute to such complications. In this studies, the ocular complications were minor and easily managed medically.

Surgical excision using the bare sclera technique is simple, requires no special skill or experiences and has less conjunctival manipulation compared to the conjunctival autograft technique. Cauterization is done during surgery, to avoid neovascularization and granulations. The use of single dose 0.04% MMC is economic and safe to avoid adverse reactions of MMC.

Both methods of MMC application with simple surgical excision were found to be safe and effective in minimizing pterygium recurrence. The single, intraoperative application of MMC would seem to be a useful and effective alternative therapeutic option in the treatment of pterygium. This treatment modality should be investigated further to determine its optimal dose and exposure time as well as its long-term safety.

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CONCLUSION

Forty four patients with pterygium underwent bare sclera technique and received 0.04% MMC topical intraoperative, 13.67% recurred. The other group of 44 patients who received 0.04% MMC topical post-operative, 15.91% recurred. However, these differences were not statistically significant (X² = 0.0902, p > 0.05).

Among the intra-operative group, there were 3 patients with pain and tearing, 2 patients with lid edema as adverse reactions, and none was found in the postoperative group. Superficial punctate keratitis was found higher in the postoperative group. No serious ocular and systemic complications in either group. A single dose intraoperative administration of MMC is a simple, economic, effective alternative therapeutic option in the treatment of pterygium. To date, there has been no evidence of scleral complication and visual loss. Because this study was relatively short, further studies is needed to determine the long-term results.

REFERENCES