

Effectiveness of subconjunctival mitomycin-C compared with subconjunctival triamcinolon acetonide on the recurrence of progresive primary pterygium which underwent Mc Reynolds method

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ABSTRACT

Donny W Chandra, Agus Supartoto, Angela Nurini Agni.- *Effectivity of subconjunctival mitomycin-C compared with subconjunctival triamcinolon acetonide on the recurrence of progresive primary pterygium which underwent Mc Reynolds method*

Background: The main problem in the management of pterygium is how to diminish the recurrence rate after surgical treatment. Mitomycin-C an antineoplastic, antifibrotic has been used to prevent recurrence rate of pterygium after excision, however, it correlated with some complications. Subconjunctival administration before excision has been proposed to avoid them.

Objective: To know the effectivity of subconjunctival of mitomycin-C to decrease the recurrence rate of progresive primary pterigyum after Mc Reynold method compared with subconjunctival triamcinolon acetonide.

Materials and methods: Randomized clinical trial of 41 progresive primary pterygium in Dr Sardjito Hospital and Dr Yap Eye Hospital. They were randomly assigned to receive subconjunctival 0.1 ml triamcinolon acetonide or 0.1 ml mitomycin-C and underwent pterygium excision one week later using Mc Reynold method. The follow up period was 6 months to detect any recurrence and complication of the drugs

Results: The recurrence rate after subconjunctival mitomycin-C and triamcinolon acetonide was 4.7% and 25%, respectively, however the different was not statistically significant ($p=0.67$). There were no statistical difference in conjunctival hiperemia, lacrimation and granulation. Blepharospasm was significantly different in seven days. The pain after injection and after excision was statistically different between two two groups.

Conclusion: The recurrence rate of progresive primary pterygium in triamcinolon acetonide group was higher than mitomycin-C group but there was no statistical difference.

Key words : Progresive primary pterygium – mitomycin-C – triamcinolon acetonide – Mc Reynold method

ABSTRAK

Donny W Chandra, Agus Supartoto, Angela Nurini Agni : **Perbandingan hasil guna mitomycin C subkonjungtiva dengan triamcinolon subkonjungtiva terhadap kekambuhan pterigium primer progresif yang dioperasi dengan metoda Reynolds**

Latar belakang: Masalah utama dalam penanganan pterigium adalah bagaimana mengurangi kejadian kekambuhan setelah operasi. Mitomycin-C bersifat antineoplastik dan antifibrotik telah diketahui dapat menghambat kejadian kekambuhan, tetapi berkaitan dengan terjadinya beberapa komplikasi. Pemberian obat secara subkonjungtiva sebelum operasi diharapkan dapat mengurangi kekambuhan tersebut.

Tujuan : Penelitian ini bertujuan untuk mengetahui hasil guna mitomycin-c subkonjungtiva dalam mengurangi kekambuhan pterigium primer progresif sebelum dilakukan operasi Mc Reynold dibanding triamcinolon acetone subkonjungtiva

Bahan dan cara: Dilakukan uji klinis acak dilakukan terhadap 41 pasien rawat jalan pterigium primer progresif di RS Dr Sardjito dan RS Mata Dr Yap. Setelah alokasi acak, dilakukan perlakuan injeksi 0,1 ml mitomycin-C atau triamcinolon asetonid subkonjungtiva dan setelah 1 minggu dilakukan eksisi dengan metode Mc Reynold. Pengamatan dilakukan selama 6 bulan untuk mendeteksi kekambuhan dan komplikasi obat.

Hasil: Kekambuhan pterigium pada kelompok perlakuan mitomycin-C dan triamcinolon asetonid subkonjungtiva masing-masing adalah 4,7% dan 25% tetapi tidak bermakna secara statistik ($p=0,67$). Tidak didapatkan perbedaan bermakna pada hiperemia konjungtiva, lakrimasi, dan pembentukan jaringan granulasi. Blefarospasme berbeda secara bermakna dalam tujuh hari. Rasa nyeri setelah injeksi dan setelah operasi pada kedua kelompok berbeda secara bermakna.

Simpulan: Angka kekambuhan pterigium primer progresif pada kelompok triamcinolon asetonid lebih tinggi daripada kelompok mitomycin-C meskipun tidak bermakna secara statistik.

INTRODUCTION

Pterygium is a growth of fibrovascular tissue from conjunctiva and subconjunctiva bulbi extending and infiltrates the surface of the cornea with apex growing toward the pupil.^{1,2,3,4,5} The growth of pterygium is flat on canthal area at the nasal side sometime to temporal side, in the form of triangle and divided into apex, collum, and corpus. Geographically, pterygium is at most found in the tropical climates. Indonesia having equator climates has high risk to develop pterygium.⁸

Pterygium is still a difficult problem and hard to overcome because of high recurrence rate post operatively.^{3,5,9,10} Recurrence rate in Indonesia is about 35 – 52%.¹¹ Research in Cipto Mangunkusumo Hospital found recurrence rate of 65% at the age below 40 years old and 12.5% at the age over 40 years old.⁸ The reason of pterygium recurrence can be explained with (1) Theory of neoplastic, (2) Theory of degeneration, (3) Theory of inflammation, and (4) Theory of immunology.^{12,13,14}

Surgery is the main treatment for pterygium. There are many variations of pterygium surgery method. The most common method used to remove pterygium is *Mc Reynold* method. In this technique

the apex of pterygium is excised and buried into conjunctival sac next to caudal limbus and it would be stitched, following the removal of subconjunctival tissue that covered cornea. It is expected that if pterygium regrowth is unavoidable would be toward conjunctival sac.

The role of steroid in suppressing leucocyte activity and decreasing vascular permeability will decrease tissue disruption, decrease mitogen and growth factor and also interrupts clot and fibrin production. This will disrupt the minimal fibroblast activity.¹⁹

Mitomycin C is an antiproliferative agent and a potent fibroblast proliferation suppressor by suppressing DNA synthesis and its function. It also acts as antineoplastic, antibiotic, and antimetabolite agent. Donnerfeld and colleagues stated that the use of preoperative subconjunctival mitomycin C was safe and effective as adjunctive therapy. It could suppress the recurrence rate with minimal complication.

The aim of this study was to know the effectiveness of preoperative subconjunctival mitomycin C compared with preoperative subconjunctival triamcinolon acetone in decreasing the recurrence rate of progressive primary pterygium removed by *Mc Reynold* method.

MATERIAL AND METHODS

This study was a randomised clinical trial. The subjects were patients who came to the Ophthalmology Departement Dr. Sardjito Hospital and Dr Yap Eye Hospital, Yogyakarta, in August 2005 - April 2007 that fulfilled inclusion criteria. The inclusion criteria were patient who had progressive primary pterygium either unilateral or bilateral, age less than 50 years old, Youngson clinical grade 2 or more, no history of eye surgery, no history of topical steroid or injection usage in last 4 weeks, no history of dry eye syndrome, willing to participate in this study by signing the informed consent. Subject was disqualified or dropped out from this study if the subject never presented to control after surgery or they did not obey the medication instruction during the study. Consecutive sampling and block randomization was performed in this study. Sample size was calculated based on Lameshow formula with recurrence rate proportion for preoperative subconjunctival triamcinolon acetonide group of 45% and recurrence rate proportion for preoperative subconjunctival mitomycin C group of 6% with assumption α was 0.05 and β was 0.20. Sample size for each group was 22. Subjects that fulfilled the inclusion criteria were asked to sign the informed consent after given explanation. History taking was performed and consisting of age, sex, occupation, disease history, medication history, history of sunblock usage before and during sun exposure. Eye examination consisted of routine ophthalmology examination, biomicroscopy examination, grading of pterygium based on Youngson, Schirmer test 1 for tear secretion function. Both groups were given tetracain hydrochloride 2% eye drop on the eye that whould be injected. Lidocain 0.1% of 0.2 mL was injected into conjunctiva until it distended with the border of apex pterygium was on limbus area and waited for five minutes. Conjunctiva was then injected with mitomycin C or triamcinolon acetonide with 0.1 mL insulin syringe. Ofloxacin 0.3% eye drop was given 4 times daily. After a week, the pterygium was excised, from the cornea widened toward upper and lower limbus. The corpus was excised by beaver blade. Undermined subconjuncti-vally inferior to cornea. Pterygium apex was inserted subconjunctivally inferior to limbus and it was sutured by silk 4.0. Foloowing surgery, every subject received ofloxacin eye drop 4 times daily and chloramphenicol eye ointment 2 times daily for one

week. Mefenamic acid 500 mg was given orally 3 times daily for a day. The patient was recommended to use eye protection such as glasses, and hat. Suture would be released on the 7th day. Recurrences were evaluated on the 14th day, and after one, two, three, and six months. Demographic data consisting of age, sex, exposure to external factor were analyzed with descriptive statistics. Recurrence rate was analyzed with chi-square test.

RESULTS AND DISCUSSION

There were 44 subjects participated in the study. Three subjects were dropped out (2 on triamcinolon acetonide group and 1 on mitomycin C group). Therefore, only 41 subjects were involved in this study.

Subject characteristics in this study consisting sex, grading of pterygium, duration of sun exposure and eye protection usage were similar mitomycin C group (35.52 ± 4.4) was significantly younger than triamcinolon acetonide group (44.2 ± 6.7 years). (TABLE 1)

TABLE 1. Subject characteristics

| Characteristic | MMC (n=21) | | TA (n=20) | | p |
|-----------------------|------------|-------|-----------|-------|-------|
| <i>Sex</i> | | | | | |
| Male | 9 | 45% | 9 | 42.8% | 0.89 |
| Female | 12 | 55% | 11 | 57.2% | |
| <i>Age</i> | | | | | |
| Average (SD) | 38.52 | 4.4 | 44, 2 | 6.7 | 0.03 |
| ≤ 40 year old | 7 | 33.3% | 16 | 80% | 0.03 |
| > 40 year old | 14 | 66.7% | 4 | 20% | |
| <i>Grading</i> | | | | | |
| Grade 2 | 18 | 85.7% | 17 | 85% | 0.94 |
| Grade 3 | 3 | 14.3% | 3 | 15% | |
| Grade 4 | - | - | - | - | |
| <i>Exposure</i> | | | | | |
| < 2 hours / day | 5 | 25% | 7 | 33.3% | 0.845 |
| 2 – 4 hours / day | 5 | 25% | 5 | 23.8% | |
| 4 – 5 hours / day | 4 | 20% | 5 | 11.9% | |
| > 5 hours / day | 6 | 30% | 4 | 19% | |
| <i>Eye protection</i> | | | | | |
| Yes | 17 | 85% | 20 | 95.2% | 0.269 |
| No | 3 | 15% | 1 | 4.7 | |

Note : MMC : Mitomycin-C, TA : Triamcinolon acetonide, SD : Standard deviation

Recurrence rate after six month evaluation in mitomycin C was lower (one case or 4.7%) compared to triamcinolon acetonide group (five cases or 25 %)

eventhough it was not statistically significant ($p=0.067$).

Recurrence time for mitomycin C group was slightly longer (three months) compared with the average recurrence time for triamcinolon acetonide group (2.8 ± 0.4 months) eventhough no statistical significant difference was found ($p>0.05$). Triamcinolon acetonide group showed greater risk of recurrence than mitomycin C group (OR = 1.94; 95%CI=1.15–3.28). However this value was influenced by age factor distribution of both groups.

In order to gain recurrence risk for both group by eliminate age predisposing factor, summary odds ratio with Mantell Haenzel was done with OR value=11.635 (95%CI=0.61-220.15) and p value=0.21, statistically not different. 95%CI showed clinically inconclusive, but it showed the tendency of difference. This was due to too small sample size. Recurrence proportion for mitomycin C group was 6% and for triamcinolon acetonide group was 45% that cause difference of 4% compared with 25% lead to not statistically significant different. In this study the power was 55.8%. It means there was 41.2% for type 2 error.

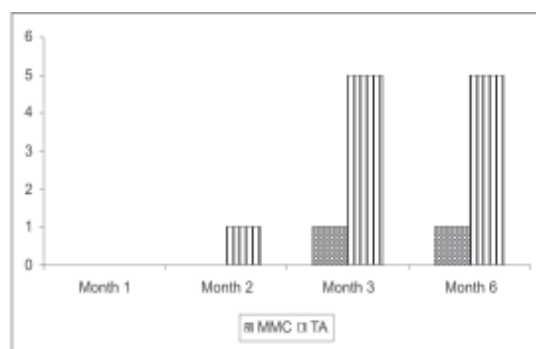


FIGURE 1. Pterygium recurrences in 6 month evaluation.

Asfani *et al.* found that recurrence rate for pterygium injected with mitomycin C subconjunctivally durante excision surgery was 13.8% compared with triamcinolon acetonide subconjunctivally was 17.2%.¹⁸ Donnenfeld *et al.* in their study reported that recurrence rate in pterygium injected with 0.1 mL mitomycin C subconjunctivally preoperative was 6% with recurrence time appeared in a month. In this study, recurrence rate in mitomycin-C subconjunctiva preoperative was 4.7%, lower compared to study of Asfani *et al.* and of Donnenfeld *et al.* Recurrence time in this study (3 month) was longer than Donnenfeld study (1 month).¹⁷

In this study, hyperemia of conjunctiva in mitomycin C group was not statistically significant different compared with triamcinolon acetonide group on 7th ($p=0.30$) vs 14th ($p=0.22$) day. Lacrimation for mitomycin C group was not statistically significant different compared with triamcinolon acetonide group on 7th ($p=0.315$) vs 14th day ($p=0.07$). Blepharospasm in mitomycin C group was statistically significant different compared with triamcinolon acetonide group on 7th day ($p=0.001$) but it was not significant different on 14th day ($p=0.067$). Subject of mitomycin C group felt more painful compared with triamcinolon acetonide group. Pain sensation was measured with visual analog scale whereas average rate of pain sensation for mitomycin C was 2.19 ± 0.67 and triamcinolon acetonide group was 1.7 ± 0.65 . In our study, pain sensation for both group were statistically significant different post antimetabolites injection ($p=0.024$), on 7th day ($p=0.029$), 14th day ($p=0.024$). Granulation was not statistically significant different for both groups ($p=0.32$), eventhough the granulation occurred in one patient of mitomycin C group. This complication probably can be caused by the usage of 4.0 silk suture that eventhough *nonantigenic* and *nonpyrogenic* irritation reaction was common. No granulation in triamcinolon acetonide group.

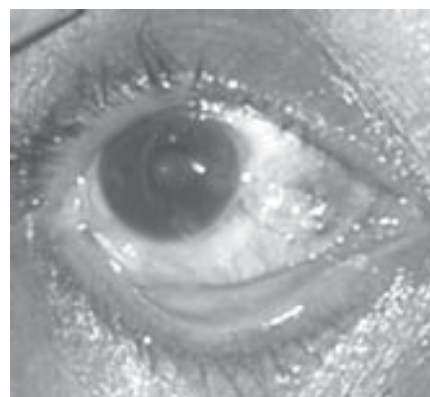


FIGURE 2. Hyperemia conjunctiva on 7th day post operative in progressive primary pterygium which injected triamcinolon acetonide.

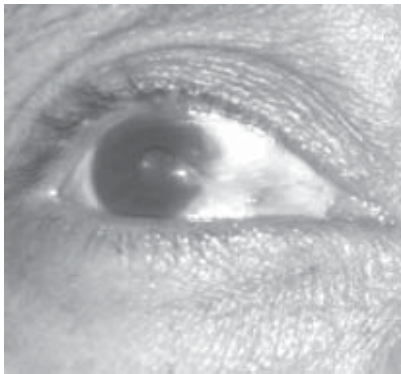


FIGURE 3. Pterygium recurrence in triamcinolon acetonide group after 3 month follow up.

CONCLUSION

Recurrence rate for triamcinolon acetonide subconjunctiva group was clinically higher compared to mitomycin-C group in progressive primary pterygium patients, eventhough no statistical significant difference. Average recurrence time in triamcinolon group was slightly faster compared to mitomycin C group, but not statistically significant different. Probability recurrence for triamcinolon acetonide group was 11.6 times than mitomycin C group with OR value 11.6 (95%CI=0.61-220.1).

There was no statistically significant difference for conjunctival hyperemia, and lacrimation on 7th and 14th day. Blepharospasm was significant different on 7th day, but not on 14th day. Pain sensation was statistically significant different post injection, on 7th, 14th day after surgery ($p < 0.05$). Patients injected with mitomycin C felt more painful than triamcinolon acetonide group Granulation occurred in one patient (4.7%) mitomycin C group but not found in triamcinolon group.

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