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## Single application of Mitomycin C in pterygium surgery

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*In an effort to search for a simple and cost-effective treatment modality for pterygium while minimizing previously known complications, seventy-five eyes were randomly selected to receive either beta radiation or single applications of 0.5 mg/ml Mitomycin C for 5 minutes as an adjunct to pterygium excision with bare scleral technique. We compared the efficacy in reducing recurrence of pterygia and complications which might occur. Fifteen eyes in the beta radiation group and 26 eyes in the mitomycin C group were followed up to 12 weeks postoperatively. The recurrence in the radiation group was 46.67% which was not statistically different from the 42.30% of the mitomycin C group. Postoperative symptoms and signs of photophobia, tearing, conjunctival hyperemia, subconjunctival hemorrhage, lid edema, superficial punctate keratitis, new vascular loop, and corneal thinning were comparable between both groups. We concluded that single application of mitomycin C was as efficient and safe as the more costly beta radiation treatment as an adjunctive therapy to pterygium excision. This is the first report using mitomycin C in a single application and comparison to beta radiation in the treatment of pterygium.*

**Key words:** Pterygium, Mitomycin-C, Recurrence, Beta-radiation.

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ปริญญ์ โรจนพงศ์พันธุ์, ชัยยะ เอี่ยมอารีรัตน์, กิตติยา มหามงคล, จุไรรัตน์ วัจนะมงคล. การใช้ยาไมโตมัยซิน ซี วางเพียงครั้งเดียวหลังการผ่าตัดต่อเนื้อ เปรียบเทียบกับการใช้รังสีเบต้า. จุฬาลงกรณ์เวชสาร 2537 กันยายน; 38(9): 529-535

ต่อเนื้อเป็นโรคที่พบได้บ่อยในประเทศไทย การผ่าตัดลอกต่อมักจะประสบปัญหาของการเกิดซ้ำใหม่ค่อนข้างสูง การใช้รังสีเบต้าหลังผ่าตัดเป็นวิธีที่ยอมรับ แต่มีราคาสูง การใช้ยาไมโตมัยซิน ซี เจือจางในรูปยาหยอดติดต่อกันหลาย ๆ วัน สามารถลดการเป็นซ้ำได้ดี แต่มีภาวะแทรกซ้อนสูง เพื่อศึกษาหาวิธีที่ประหยัด ได้ผลดีและมีภาวะแทรกซ้อนต่ำในการป้องกันการเกิดขึ้นซ้ำใหม่ของต่อเนื้อ ผู้วิจัยได้ทดลองใช้ ไมโตมัยซิน ซี ความเข้มข้น 0.5 mg/ml วางเพียงครั้งเดียว นาน 5 นาที เปรียบเทียบกับการวางรังสีเบต้าในผู้ป่วยต่อเนื้อ หลังทำการผ่าตัดด้วยวิธี bare scleral โดยการสุ่มผู้ป่วยจำนวน 15 คน เข้ารับการรักษาร่วมด้วยรังสีเบต้า และอีก 26 คน ได้รับการรักษาด้วย ไมโตมัยซิน ซี หลังจากทำการผ่าตัดลอกต่อเนื้อออก ผลการศึกษาพบว่า อัตราการเป็นซ้ำในกลุ่มแรกเท่ากับ 40.67% ซึ่งไม่แตกต่างกันทางสถิติจาก 42.30% ของกลุ่มหลัง โดยติดตามผู้ป่วยเป็นเวลา 12 สัปดาห์ นอกจากนี้ยังพบว่าไม่มีความแตกต่างกัน ในแง่ของภาวะแทรกซ้อนในระหว่างผู้ป่วยสองกลุ่ม และไม่พบภาวะแทรกซ้อนที่สำคัญในกลุ่มที่ใช้ไมโตมัยซิน ซี ผลจากการศึกษาทำให้สามารถสรุปได้ว่าการใช้ยา ไมโตมัยซิน ซี วางเพียงครั้งเดียวหลังผ่าตัดต่อเนื้อ เป็นวิธีที่สามารถให้ผลในการลดอัตราการเป็นซ้ำได้ดีพอกับการใช้ beta radiation และไม่พบภาวะแทรกซ้อนที่รุนแรง และถือเป็นรายงานฉบับแรกที่ศึกษาการใช้ มัยโตมัยซิน ซี เพียงครั้งเดียว ในการผ่าตัดต่อเนื้อ

Pterygium is among the most common eye diseases in Thailand and other tropical countries. Many procedures have been used for removing pterygium with widely varying degrees of success. Simple excision results in an unacceptable high incidence of recurrence which can be as high as 89%.<sup>(1)</sup> Use of beta radiation after surgical excision of pterygia has been shown to reduce the recurrence rate to 5-12%.<sup>(2,3)</sup> However there is a problem of availability of the radiation treatment due to its high cost. Mitomycin C is an antibiotic-antineoplastic agent which has been reported to reduce the recurrence of pterygium to 2-13%<sup>(1,4-6)</sup> after excision. Several serious complications related to mitomycin C treatment have been reported,<sup>(7-9)</sup> of which employed multiple dosage regimen. However, less complications were reported with lower concentrations and less frequent drops<sup>(6)</sup> but with a lower success rate.<sup>(5)</sup>

In recent years single application of mitomycin C has been effectively used as an adjunctive anti-fibroblastic agent in glaucoma surgery.<sup>(10-12)</sup> Early experience by one of us (PR) with single application of mitomycin C after pterygium surgery showed encouraging results (unpublished data). It was not known whether single application of mitomycin C would be as effective as standard beta radiation in terms of recurrence rate and safety. This prompted us to investigate this treatment modality in a randomized control prospective study.

### Material and methods

Primary pterygia in seventy-five eyes from 75 patients were surgically excised by us (CA., KM. and JW.) from August to November 1993. Twenty-nine eyes were

randomized to be treated with beta radiation and the remaining 46 were treated with single application of mitomycin C at a concentration of 0.5 mg/ml for 5 minutes after the bare scleral technique for excision of pterygia. The diagnosis of primary pterygium was determined by clinical findings. Patient history and examination records of inflammation, vascularity, the length of pterygium growing into the cornea from limbus, and the width of pterygium base at the limbus were noted. All the surgical excisions were performed on an outpatient basis in the following manner: 1) conjunctival anesthesia achieved with 0.5% proparacaine hydrochloride, 2) after placement of lid speculum, a subconjunctival injection of 0.1-0.2 ml of 2% lidocaine with 1:200,000 epinephrine was injected into the body of the pterygium with a 27-gauge needle, 3) the pterygium was dissected with scissors and a #15 surgical blade to leave the bare sclera exposed with or without suturing the conjunctival edge, and 4) a pressured eye patch was applied after instillation of antibiotic steroid ointment (Sofradex<sup>R</sup> eye ointment).

The surgical nurse randomized any patient who was scheduled to have pterygium excision to receive either mitomycin C or beta radiation treatment. Mitomycin C was freshly prepared by mixing 2 mg. vial (Kyowa pharmaceutical, Japan) with 4 ml distilled water as the diluent to make 0.5 mg/ml solution. A small piece of cotton was then soaked with the solution and placed on the bare sclera covering the conjunctival excised edge. After 5 minutes, the area was irrigated with 50 ml normal saline. In the beta radiation group, application of 2,000 rads on the bare sclera was carried out after pterygium excision. All eyes were patched firmly for 24 hours

and examined on the next day. Scheduled follow-up evaluations were at 1,2,4,8 and 12 weeks post-operation. The symptoms and signs included photophobia, tearing, hyperemia, and superficial punctate keratitis which persisted more than 1 week, and conjunctival hemorrhage, which lasted more than 2 weeks. Examination of new vascular loop, corneal thinning and recurrence of fibrovascular tissue beyond the limbus were noted on each visit. All information was recorded on a prepared form.

### Results

There were 29 eyes in the beta radiation treated group and 46 eyes in the mitomycin C treated group. After 12 weeks, 14 patients in the radiation group and 20 patients in the

mitomycin C group were lost to follow-up. The remaining 41 cases were compared and analyzed. The mean age, sex distribution, the degree of vascularization of pterygium, and the length of pterygium from limbus into the cornea of both groups were compared. None of these parameters were statistically different between the two groups (Table 1.) It was determined that the mitomycin C group had significantly greater degrees of inflammation ( $p < 0.03$ , chi-square test) and greater width of pterygium body at limbus ( $p < 0.04$ , student's t-test). Seven of the 15 eyes (46.67%) in the beta radiation group had recurrence and 11 of the 26 eyes (42.3%) of the mitomycin C group had recurrence. The difference was not statistically significant.

**Table 1.** Baseline characteristics of patients.

Character	Group 1 Mitomycin-C	Group 2	p value
Beta - radiation			
No. of eyes	15	26	-
Mean age (yrs.)	38.5 + 12.5 (20-59)	42 + 17.6 (15-80)	NS
Sex (M:F)	4:11	10:16	NS
Inflame (%)	27	66	$p = .03$
Vascular (%)	67	66	NS
Length from limbus (mm) <sup>2</sup>	2.8 + 0.9	3.44 + 1.6	NS
Base at limbus (mm)	4.8 + 1.1	5.4 + 2.1	$p = .04$

Statistical evaluation using Chi-square test and student's t test.

Most patients in both groups had symptoms of photophobia and tearing and signs of conjunctival hyperemia and/or hemorrhage of varying degrees for 1 to 2 weeks post-operatively (Table 2). We found no statistically significant difference when comparing the following symptoms and

signs of the two groups : photophobia, tearing, conjunctival hyperemia, subconjunctival hemorrhage, lid edema, superficial punctate keratitis, and new vascular loop on post-excision bare sclera. There was no corneal thinning noted in the study.

**Table 2.** Complications and Recurrence after treatment.

Group 1 Complications	Group 2		p value
	Beta-radiation	MMC	
No. of eyes	15	26	-
Photophobia > 1wk(%)	60.0	26.9	NS
Tearing > 1wk(%)	26.7	15.4	NS
Hyperemia > 1wk(%)	66.7	61.5	NS
Conjunctival hemorrhage > 2wk(%)	13.3	3.8	NS
Lid edema > 1wk(%)	0	7.7	NS
SPK > 1wk(%)	6.7	7.7	NS
New vascular loop (%)	6.7	30.7	NS
Corneal thinning (%)	0	0	-
Recurrence (%)	7 (46.67)	11 (42.30)	NS(p=.96)

Statistical evaluation using Chi-Square test.

## Discussion

This is the first study of single application of mitomycin C in pterygium surgery when comparing its efficacy and safety to the standard treatment modality of beta radiation. The recurrence rates and significant complication rates were comparable among both groups.

Preoperative parameters were comparable between both groups, except for the degree of pterygium inflammation and the width of the pterygium body at limbus, which were significantly greater in the mitomycin C group. It is well known that the greater degree of inflammation, the more chances of recurrence. The greater width of the pterygium body would indicate a more advanced status of disease. Therefore, this would suggest that intraoperative single application of mitomycin C was as efficient as beta radiation, if not better.

The recurrence rates in this study

were rather high in both groups when compared to other previous studies using multiple-drop regimen.<sup>(1,5,6)</sup> However, the patients in our study were younger than in some previous reports,<sup>(1,6)</sup> and they also, higher degrees of inflammation and vascularity which indicated a more active disease status. With our randomized trial, we demonstrated that the efficacy and safety of single applications of mitomycin C was as good as the more costly beta radiation.

The single application of mitomycin C has the advantage of simple application and the nationwide availability of mitomycin C. It is also more economical. The effectiveness of it has been impressively shown by previous clinical studies with dosages of 0.1% to 0.02% solution, 3 to 4 times daily for 5 to 14 days.<sup>(1,5,6)</sup> However, severe complications including secondary glaucoma, corneal edema, corneal perforation, correctopia, iritis, sudden onset of mature cataract, scleral perforation

and incapacitating photophobia and pain were reported.<sup>(7-9)</sup> In our study of single application of mitomycin C, which greatly reduced the frequency and contact duration of the agent to the ocular tissue, we found no significant complications. It is possible that the follow-up period reported in our study was rather short and corneal thinning or scleromalacia complication may be experienced later. A longer follow-up is needed to further document this treatment modality. It is not known whether adjusting the concentration or duration of mitomycin C application will yield a better result. It is also not known if a combination of single application of mitomycin C with other treatment modalities will be more beneficial. All of these need to be examined by further studies. It is desirable to find the lowest optimal concentration and the shortest application time which will be of most benefit in the reduction of recurrence but prevent serious complications.

In conclusion, we have first shown that single application of mitomycin C is at least as effective as beta radiation in preventing post-operative recurrence of pterygium. The technique is simple, and avoids the need of patient cooperation to take the drop and this possibly avoids consequential complications which might occur. Although we did not observe severe complications in any patient, a longer follow-up is required before reaching final conclusions. Further studies to of a larger group modify the dosage are needed.

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