A Comparison of Trabeculectomy Outcomes by Intratenon Injection Mitomycin-C Versus Soaked-Sponge-Applied Mitomycin-C: One-year Follow up

Sutee Ananprasert, Naruechanok Lertkusol, Luksamon Pas-arj

Department of Ophthalmology, Thammasat University Hospital, Thailand

Abstract

Objectives: To compare the efficacy and safety of mitomycin-C (MMC) injected intratenon with conventional soaked-sponge-application in trabeculectomy.

Materials and Methods: We retrospectively reviewed 90 patients with primary and secondary glaucoma diagnoses who received trabeculectomy surgery with MMC in Thammasat University Hospital, Thailand from 2018 to 2021. The MMC was administered to the subjects via either an intratenon injection or a soaked-sponge-application. Postoperative intraocular pressure (IOP) level was the primary outcome measure, with survival rates for IOP control, number of glaucoma medications used, complication rates, and vision serving as secondary outcomes.

Results: There were 90 eyes available for analysis; 36 eyes had MMC delivered via intratenon injection and 54 eyes via soaked-sponge. Mean preoperative IOP in intratenon group was 28.44 ± 12.87 mmHg and soaked sponge-applied group was 26.83 ± 6.51 mmHg, which reduced to 14.72 ± 10.08 and 11.63 ± 3.76 mmHg at final visit with *P* value of 0.373, respectively. Mean preoperative number of antiglaucoma medications was 3.64 ± 0.54 in intratenon group and 3.70 ± 0.54 in soaked-sponge-applied, which reduced to 0.78 ± 1.07 and 0.30 ± 0.82 with *P* value of 0.007, respectively. Overall, success rate (complete + qualified) was 80.6% in intratenon injection and 96.3% in soaked-sponge-applied at final visit with *P* value of 0.030, respectively. There was no difference between groups in postoperative complications including choroidal effusion, over filtration, hypotony, malignant glaucoma, bleb leak and blebitis ($p > 0.05$). The time to failure for postoperative IOP control was significantly different between groups. There was a higher survival rate of the soaked-sponge-applied group than intratenon group.

Conclusions: Both MMC delivery methods are effective in reducing IOP and the number of antiglaucoma medications. However, the sponge-applied group demonstrated superior success rates without an increased risk of complications.

Keywords: Intratenon injection mitomycin-C, Soaked-sponge-applied mitomycin-C, Trabeculectomy

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Introduction

Glaucoma is one of the most common causes of irreversible blindness around the world.[1] The loss of sight from glaucoma significantly affects the quality of life (QoL). Therefore, screening and proper treatment by ophthalmologists is greatly important to early detect and preserve remaining vision.

Nowadays, a variety of glaucoma treatments depend on many factors, such as type of glaucoma, severity of disease, socioeconomic status. The choice of treatment consists of topical medication, laser and surgery.

Correspondence to:
Sutee Ananprasert, *Department of Ophthalmology, Thammasat University Hospital, Thailand*
E-mail: sutee_bird13@hotmail.com
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Trabeculectomy is a standard surgical procedure for glaucoma. It bypasses the fluid out of the eye to the subconjunctival space to reduce intraocular pressure (IOP)[2] into optimal levels which is important in glaucoma treatment.

However, trabeculectomy alone has a slightly high failure rate. In the 1990s, Mitomycin-C (MMC), from actinobacteria streptomyces caespitosus[3], was used with trabeculectomy.[4] It can inhibit cell proliferation in inflammatory processes and prevent scar formation.

There were many ways to use mitomycin-C in glaucoma surgery. For example, using amnion membrane with MMC[5]or Soaked-sponge-applied MMC.[6] Nevertheless, the latter associated with bleb leak and infection.[7, 8]

The intratenon injection of mitomycin-C in adjuvant trabeculectomy was invented in 2008 by Lee E, et al. This was a retrospective, single arm study. It shows an effective technique that compares with others.[9] In 2017, There were several comparative studies showing the superior outcomes of the intratenon route over the traditional soaked-sponge technique. Two studies suggested that bleb morphology is more favourable[10, 11] and another shows more IOP reduction in the intratenon group.[12]

At Thammasat University Hospital, a tertiary center in Thailand, we used both techniques to apply MMC in trabeculectomy. And this is our comparative study with regards to treatment outcomes.

Methods and Methods

It is a descriptive study, a retrospective chart review with the patients diagnosed with primary or secondary glaucoma (n = 90) who received limbal based trabeculectomy surgery with mitomycin-C (MMC) used either intratenon injection route (0.1-0.2 mg/ml of mitomycin-C 0.1 ml) or soaked-sponge-applied (0.4 mg/ml of mitomycin-C for three minutes) in Thammasat University Hospital from January 2018 to June 2021. The exclusion criteria were age less than 18 years old, no light perception vision and the patients who have undergone previous incisional glaucoma surgery.

All patients underwent comprehensive ocular examinations such as best-corrected visual acuity, intraocular pressure by Goldmann applanation tonometry, fundus examination. We collected age, sex, the cause of glaucoma, laterality, underlying diseases, route of applied mitomycin-C, status of lens Intraocular pressure and number of glaucoma medications, postoperative interventions, and postoperative complications at each visit until one year.

We used the Fisher Exact test for categorical data and Mann-Whitney U-test for continuous data. The survival times of intraocular pressure (IOP) control was analyzed by Kaplan-Meier and reported as a survival curve.

This study was approved by the Thammasat University Hospital Human Ethics Committee and performed in accordance with the Declaration of Helsinki.

Results

There were 90 eyes included in this study, 36 eyes had mitomycin-C (MMC) delivered via intratenon injection and 54 eyes via soaked-sponge-application. The baseline characteristics (age, sex, underlying disease, laterality, cause of glaucoma, visual acuity, baseline IOP, number of medications, and lens status) were not statistically significant between both groups.

Table 1: Baseline characteristics of the subjects (n = 90)

Characteristics	Total (n=90)		Intratenon MMC (n=36)		Soaked Sponge (n= 54)		p-value
	n	%	n	%	n	%	
Sex							0.710
Male	62	68.9%	24	66.7%	38	70.4%	
Female	28	31.1%	12	33.3%	16	29.6%	
Age (years)							
Mean±SD.	62.98	±14.59	58.86	±17.02	65.72	±12.13	0.100
Medical history							0.114
yes	54	60.0%	18	50.0%	36	66.7%	
Diabetes	31	34.4%	10	27.8%	21	38.9%	0.277
Hypertension	37	41.1%	13	36.1%	24	44.4%	0.431
Hypercholesterolemia	22	24.4%	10	27.8%	12	22.2%	0.548
Chronic kidney disease	7	7.8%	5	13.9%	2	3.7%	0.111
Glaucoma diagnosis							0.501
Primary open-angle glaucoma	21	23.3%	11	30.6%	10	18.5%	
Primary angle-closure glaucoma	33	36.7%	13	36.1%	20	37.0%	
Secondary open-angle glaucoma	14	15.6%	6	16.7%	8	14.8%	
Secondary angle-closure glaucoma	20	22.2%	5	13.9%	15	27.8%	
Other/combined	2	2.2%	1	2.8%	1	1.9%	
Preoperative visual acuity (logMAR), mean±SD	1.37	±1.12	1.41	±1.31	1.34	±0.99	0.484
Baseline IOP (mm Hg), mean±SD.	27.48	±9.54	28.44	±12.87	26.83	±6.51	0.533
Baseline medications, mean±SD	3.68	±0.54	3.64	±0.54	3.70	±0.54	0.485
Lens status							0.162
Phakia	37	41.1%	18	50.0%	19	35.2%	
Pseudophakia	53	58.9%	18	50.0%	35	64.8%	

p values for mean data were calculated with the use of Man-Whitney U- test, for percentages with the use of Chi-square test or Fisher's exact test, * Significant at p-value < 0.05

Table 2: Results comparison between intratenon VS soaked-sponge route of mitomycin-C delivery.

	Intratenon MMC (n=36)	Soaked Sponge (n= 54)	Difference		p-value
	Mean ±S.D.	Mean ±S.D.	Mean	(95% CI)	
Mean IOP (mm Hg)					
Preoperative baseline	28.44 ±12.87	26.83 ±6.51	1.61	(-3.06 ,6.28)	0.533
3 months	12.47 ±6.91	11.39 ±4.21	1.08	(-1.25 ,3.41)	0.652
6 months	14.61 ±10.03	10.65 ±3.59	3.96	(0.45 ,7.48)	0.146
1 year	14.72 ±10.08	11.63 ±3.76	3.09	(-0.45 ,6.64)	0.373
Visual acuity					
Preop	1.41 ±1.31	1.34 ±0.99	0.07	(-0.44 ,0.58)	0.484
3 months (n=89)	1.33 ±1.23	1.18 ±0.89	0.15	(-0.33 ,0.63)	0.566
6 months (n=88)	1.33 ±1.30	1.22 ±0.91	0.11	(-0.40 ,0.61)	0.352
1 year (n=85)	1.13 ±1.13	1.28 ±0.88	-0.15	(-0.62 ,0.32)	0.028*
Medications					
Preoperative baseline	3.64 ±0.54	3.70 ±0.54	-0.06	(-0.30 ,0.17)	0.485
3 months	0.33 ±0.83	0.09 ±0.35	0.24	(-0.05 ,0.54)	0.147
6 months	0.53 ±1.11	0.22 ±0.63	0.31	(-0.10 ,0.71)	0.296
1 year	0.78 ±1.07	0.30 ±0.82	0.48	(0.06 ,0.90)	0.007*

p-value from Man-Whitney U- test, * Significant at the 0.05 level

Mean preoperative intraocular pressure (IOP) in intratenon group was 28.44 ± 12.87 mmHg and sponge-applied group was 26.83 ± 6.51 mmHg, which reduced to 14.72 ± 10.08 and 11.63 ± 3.76 mmHg at the final visit with p-value of 0.373, respectively.

Mean preoperative number of antiglaucoma medication was 3.64 ± 0.54 in the intratenon group and 3.70 ± 0.54 in the sponge-application group, which reduced to 0.78 ± 1.07 and 0.30 ± 0.82 with p-value of 0.007, respectively

The complete success rate was 69.0% in the intratenon route and 88.5% in the sponge-applied route at the end of one year. Overall success rate (complete+qualified) was 80.6% and 96.3% in intratenon and sponge-application group at last visit with p-value of 0.03, respectively.

Graph 1: Shows average intraocular pressure (IOP) reduction after the surgery in both groups.

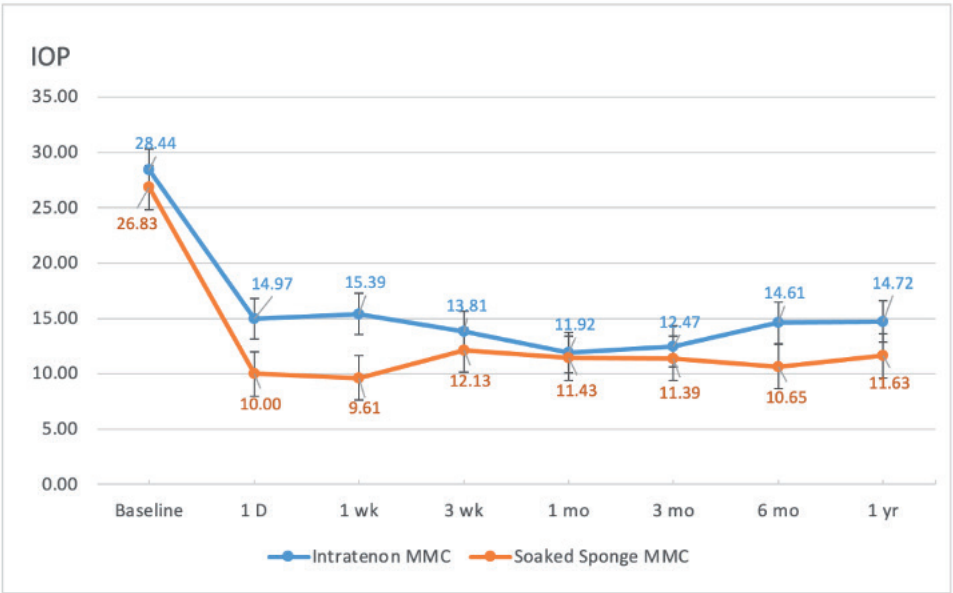


Table 3: Complications and Intervention (n = 90)

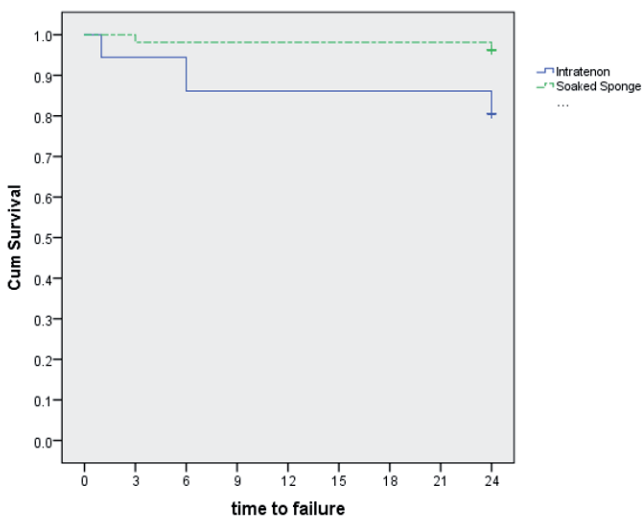
The IOP difference was not statistically significant at all study time points.

	Intratenon MMC (N=36)		Soaked Sponge (N= 54)		p-value
	N	%	N	%	
Complication 1 month					0.171
Yes	6	16.7%	4	7.4%	
Choroidal effusions	1	2.8%	1	1.9%	
Over filtration	1	2.8%			
Hypotony	2	5.6%	2	3.7%	
Malignant glaucoma	1	2.8%			
revised	1	2.8%			
Bleb leak			1	1.9%	
no	30	83.3%	50	92.6%	
Complication greater than 1 month					0.315
Yes	5	13.9%	4	7.4%	
no	31	86.1%	50	92.6%	
Hypotony	1	2.8%	2	3.7%	
No light perception vision	4	11.1%	1	1.9%	
Reoperation for uncontrolled glaucoma			1	1.9%	
Interventions					0.009*
yes	22	61.1%	18	33.3%	
no	14	38.9%	36	66.7%	
Number of Intervention					0.049*
0	14	38.9%	36	66.7%	
1	12	33.3%	10	18.5%	
2	6	16.7%	5	9.3%	
3	2	5.6%	3	5.6%	
4	2	5.6%	0	0%	

p values from Chi-square test or Fisher's exact test, * Significant at the 0.05 level

There was no difference between groups in minor postoperative complications including choroidal effusion, overfiltration, hypotony, malignant glaucoma, bleb leak ($p > 0.05$). No patients in either group had severe complications, such as bleb infection, endophthalmitis after the surgery. Nonetheless, not only the number of intervention after surgery was higher in the intratenon group, but also there were four patients who experienced no light perception vision in the intratenon compared with only one patient in soaked-sponge group.

Graph 2: Survival rate of intraocular pressure (IOP) control at first year: 80.6% of intratenon group VS 96.3% of soaked-sponge group ($p = 0.015$)



Time to failure for postoperative intraocular pressure (IOP) control was significantly different between MMC treatment arms with p = 0.015. The higher survival rate in the soaked-sponge-application group suggests that this MMC delivery method is associated with better IOP control at the end of the first year compared to the intratenon route (The failure was defined by IOP > 21 mmHg or decline less than 20% from baseline).

Discussion

There were many comparative studies showing the similarity of results in terms of IOP lowering and safety profile between intratenon injection and soaked-sponge application MMC in trabeculectomy.[11-13] That was harmonious with our results showing IOP lowering efficacy was similar.

Nevertheless, the survival rate of intraocular pressure (IOP) control at first year in the intratenon group was lower than the soaked-sponge group (p = 0.015). The reason might be a high scar formation at scleral flap because scleral flap may not have a good exposure to mitomycin-C in the intratenon group. And in terms of the safety profile, we found it was lower in the intratenon group due to four patients who experienced no light perception vision in the intratenon group compared with only one patient in the soaked-sponge group.

Furthermore, our research shows the number of glaucoma medications and number of interventions after surgery were higher in the intratenon group than the soaked-sponge group with p = 0.007 and 0.09 respectively.

The main limitation of this study was its retrospective design, and the causes of glaucoma might play an important role in final outcomes. Moreover, the fact that several surgeons performed the surgery and followed up the patients might also affect the result of the study.

Conclusion

The trabeculectomy with mitomycin-C (MMC) procedure is still the practical standard glaucoma surgery. Moreover, both MMC delivery routes are effective in reducing IOP and the number of antiglaucoma medications. However, the sponge-applied route demonstrated superior success rates without an increased risk of complications.

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