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Pterygium Excision with Application of Mitomycin C in Comparison to Sub-Pterygium Injection of Avastin without Excision

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Abstract

Pterygium is an ocular surface degenerative lesion presenting as a wing shaped fibrovascular conjunctival growth. It is located at the interpalpebral region of the conjunctiva, mostly nasal and extends to the cornea. Its prevalence has been reported to range from 0.3 to 29% and is mainly found in the tropical region. To discuss the outcomes and benefits for the patient in the treatment of the pterygium by excision and application of mitomycin C and sub-pterygium avastin injection without excision. The study was conducted from July 2021 till July 2022 in the Ophthalmology department of Al-Zahraa University Hospital. 40 patients who visited Ophthalmology Department at Al-Zahraa University Hospital will be included in the study. The clinical study was approved by the Azhar's University ethics committee. The follow up of all patients was done 1 week, 1 month, 3 months and 6 months postoperatively. Every follow up we examine BCVA, autorefraction, K reading. In our study we found that there is no dangerous complication in two methods of treatment however discomfort and hyperemia after 1 weeks was in all cases of group (1). Also, we found that Recurrence after one month was significantly higher in group 2. There were no significant differences between the two groups as regards the BCVA after 1, 3 and 6 months. The application of mitomycin C in comparison to sub pterygium injection of Avastin without excision are safe treatments. The two method was associated with low recurrence rates, but the use of Avastin without excision is superior in terms of complications as the mitomycin C was applied after an operation. All cases experienced discomfort after Surgery and Hyperemia for 1 week. Further comparative studies with larger sample size and longer follow up are needed to confirm the current results.

Keywords: Pterygium, Mitomycin C, Avastin

1. Introduction

Pterygium is an ocular surface degenerative lesion presenting as a wing shaped fibrovascular conjunctival growth. It is located at the interpalpebral region of the conjunctiva, mostly nasal and extends to the cornea. Its prevalence has been reported to range from 0.3 to 29% and mainly found in the tropical region. The pathogenesis of pterygium is not definite but exposure to ultraviolet light has been identified as a major risk factor for the development of pterygium. Other risk factors include chronic irritation from dust

and wind**.** An individual with pterygium may present with visual disturbance due to its induction of astigmatism or by its growth extending on the cornea to occlude the visual axis Bekibele et al., [1].

The primary treatment of pterygium is surgical excision. Various treatment modalities have been developed due to the high rate of postsurgical recurrences and adjuvant treatment methods are performed. Since the recurrent pterygium cases are more aggressive than the primary pterygium, it is of great importance to determine the treatment method with the lowest recurrence rate Hacıoğlu and Erdöl, [2].

Mitomycin C (MMC) is an alkylating agent with cytotoxic effects, which inhibits DNA synthesis and is widely used in ophthalmology. Inhibition of DNA synthesis leads to inhibition of mitoses **,** especially when MMC comes into contact with cells that are in the late G1 and early S phases of the cell cycle**.** The topical application of MMC following the excision of pterygium can reduce the rate of recurrence Alsmman et al., [3].

Pterygium presents higher levels of VEGF (vascular endothelial growth factor) compared with normal conjunctiva, so anti-VEGF drugs may be useful for pterygia patients**.** Bevacizumab (avastin) is a recombinant human monoclonal antibody against VEGF, which is approved by FDA treating neoplasms Sun et al., [4]. The efficacy of anti-VEGF treatment agents such as bevacizumab (avastin) has been evaluated in pterygium. Subconjunctival bevacizumab injection without surgery for primary pterygium was shown to be effective for reducing the pterygium size and improving visual function Zeng et al., [5].

The aim is to discuss the outcomes and benefits for the patient in the treatment of the pterygium by excision and application of mitomycin C and sub-pterygium avastin injection without excision.

2. Patients and Methods

2.1 Type of study

Cross-sectional study.

2.2 Study setting

The study was conducted at Ophthalmology department of Al-Zahraa University Hospital.

2.3 Study Period

Till the sample size was completed, from July 2021 till July 2022.

2.4 Study population

40 patients who visited Ophthalmology Department at Al-Zahraa University Hospital will be included in the study. The clinical study was approved by the Azhar's University ethics committee.

2.5 Sampling Size and Method

All 40 Study cases were classified randomly into: Group 1 (G1): Included 20 patients who underwent application of mitomycin C after pterygium surgical excision. Group 2 (G2): Included 20 patients who underwent anti-VEGF (Avastin) sub-pterygium injection without excision.

2.5.1 Inclusion criteria

Primary pterygia.

2.5.2 Exclusion criteria

Recurrent pterygium. Ocular diseases, e.g., iritis, herpetic keratitis, glaucoma, and cataract. Previous ocular surgery. Any predisposing condition to ulceration or poor wound healing, such as dry eye or atopic keratoconjunctivitis. Pregnant or lactating women.

2.6 Operative Design

All patients will be subjected to Complete history taking: Personal history Any complaint. Past medical and past surgical history. Family history. Complete ocular examination. The first Group (G1) underwent pterygium surgical excision under local anesthesia by the bare sclera technique with application of mitomycin C.

2.6.1 Bare sclera technique

Surgery was performed under microscope set at low magnification and intensity. Head of pterygium was grasped with toothed forceps at the limbus and a little pull was applied to make the dissection easy. Dissection was done using number 15 blade to free the head from the cornea. Conjunctival epithelium was bluntly dissected away from sub-epithelial tissue. Subconjunctival tissue was then excised with scissors. At the end, 3 - 4 mm of sclera was left bare. The blade was then used to clear any remnant adherent to the cornea. The corneal surface was kept as smooth as possible.

2.6.2 Application of mitomycin C

Intraoperative mitomycin was applied to the bare scleral bed for 3 minutes with a sponge supersaturated with 0.04% (0.4 mg/ml) mitomycin. The ocular surface was irrigated copiously with balanced salt solution after application. The second Group (G2) underwent anti-VEGF sub-pterygium injection. Patients underwent injection of 1.25mg/0.05 mL of Bevacizumab (Avastin) into the base of the pterygium with a 30-gauge needle in the operating room and under the microscope.

2.6.3 Injection procedures:

The injection of anti VEGF was performed under direct visualization in minor operating theatre. A sterile eyelid speculum was inserted. Anti VEGF was injected subconjunctivally in the body of the pterygium using a 30-guage needle at a dose of 1.25 mg in 0.05 ml. post-injection, a sterile cotton swab was placed at the site of injection to prevent reflux of drug. Topical antibiotic drops and ointment were used A sterile eye pad was placed that was removed 4 hours later. Patients were instructed to apply topical antibiotic drops 4 times a day for 5 days. Injections were repeated after 1 month if needed then 2 months for a maximum of 3 injections or until the desired endpoint was achieved atrophic pterygium, mild grade.

All patients were followed up and had comprehensive ophthalmic evaluation including Automatic objective determination of the refractive errors. Measurements of the best-corrected visual acuity. Photographic documentation of the pterygia was performed for each patient before and after surgery. photographs were taken from corneal surface with ×16 magnifications using a digital camera. Corneal involvements were measured on the digital photographs as the percentage of the total area of the cornea. Image analysis was performed using an image processing and analysis software program.

2.7 Administrative Design

The protocol was applied for approval of Research Ethics Committee. Informed consent was obtained from the patients before enrollment of the study. All data was kept confidential. All participants had the right to withdraw from the study without affecting their management.

3. Statistical Analysis

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges when parametric. Also, qualitative variables were presented as number and percentages. The comparison between groups regarding qualitative data was done by using Chi-square test and/or Fisher exact test when the expected count in any cell found less than 5. The comparison between two groups regarding quantitative data and parametric distribution was done by using independent t-test. The comparison between two paired groups regarding quantitative data and parametric distribution was done by using Paired t-test while with non-parametric distribution was done by using Wilcoxon test. The comparison between more than two paired groups regarding quantitative data and parametric distribution was done by using Repeated Measures ANOVA test while with non-parametric distribution was done by using Friedman test. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following: P-value > 0.05: Non-significant (NS). P-value < 0.05: Significant (S). P-value < 0.01: Highly significant (HS).

4. Results

In group 1, the age of patients ranged from 32 years to 73 years, with a mean of 44.85±12.84 years of age, in group 2, the age of patients ranged from 31 to 63, with a mean of 40.20± 8.86 years of age as shown in Table (1). There was no statistically significant difference regarding age between the two groups (P > 0.05). Regarding gender, there are 12 males (60%) and 8 males (40%) in group 1, while group 2 included 11 (55%) males and 9 (45%) females with no statistically significant difference between the two groups (P > 0.05). There was no statistically significant difference between the two groups regarding residence and occupation (P > 0.05).

Table (1). Socio-demographic characters of the studied groups.

Variable		Group 1 (N=20)		Group 2 (N=20)		Test value	P-value
		No.	%	No.	%		
Age (years)	Mean± SD	44.85±12.84		40.20± 8.86		Z_{MWU}= 0.895	0.383
	Median (IQR)	39.5 (35.5- 57.5)		38.0 (35.0- 43.0)			
	Range	32.0- 73.0		31.0- 63.0			
Gender	Male	12	60.0%	11	55.0%	X^2= 0.102	0.749
	Female	8	40.0%	9	45.0%		
Occupation	Inside	6	30.0%	8	40.0%	X^2= 0.110	0.740
	Outside	14	70.0%	12	60.0%		
Residence	Rural	3	15.0%	6	30.0%	X^2= 0.573	0.449
	Urban	17	85.0%	14	70.0%		

Table (2). Comparison between the studied groups regarding side and state of ptergium.

Variable		Group 1 (N=20)		Group 2 (N=20)		Test value	P-value
		No.	%	No.	%		
Side of ptergium	Left	10	50.0%	8	40.0%	X^2= 0.404	0.525
	Right	10	50.0%	12	60.0%		
State of ptergyuim	Fleshy	6	30.0%	6	30.0%	X^2= 0.622	0.733
	Membranous	8	40.0%	10	50.0%		
	Non-memranous, non-fleshy (moderate)	6	30.0%	4	20.0%		

***P value< 0.05 is significant, P value< 0.01 is highly significant SD: Standard deviation, IQR: Interquartile range,* X^2= Chi- Square test**

Regarding side, there are 10 (50%) located at left side and 10 (50%) located at right side in group 1, while group 2, 8 (40%) were in left side and 12 (60%) at right side with no statistically significant difference between the two groups (P > 0.05). Also, there was no statistically significant difference between the two groups regarding State of ptergyuim (P > 0.05) as there was 40% were membranous, 30% fleshy and 30% moderate in group 1 while in group 2, there was 50% were membranous, 30% fleshy and 20% moderate.

Table (3): Comparison between the studied groups regarding eye examination before intervention.

Variable		Group 1 (N=20)	Group 2 (N=20)	Test value	P-value
Visual acuity	Mean± SD	0.45±0.24	0.53±0.24	Z_{MWU}= 0.986	0.324
	Median (IQR)	0.50 (0.30- 0.50)	0.50 (0.30- 0.70)		
	Range	0.10- 1.0	0.16- 0.90		
Sphere	Mean± SD	116.90± 43.24	115.65± 33.46	Z_{MWU}= 0.895	0.383
	Median (IQR)	110.0 (92.5- 152.5)	110.0 (92.5- 152.5)		
	Range	25.0- 180.0	25.0- 180.0		
Cylinder	Mean± SD	-1.14±0.96	-0.92±0.47	Z_{MWU}= 0.553	0.580
	Median (IQR)	-1.0 (-1.50- -0.50)	-1.0 (-1.0- -0.50)		
	Range	-3.25- (0.75)	-2.0- (-0.25)		
K1. reading	Mean± SD	42.20±1.32	42.00±1.34	Z_{MWU}= 0.360	0.719
	Median (IQR)	42.0 (41.0- 43.0)	42.0 (41.50- 42.0)		
	Range	40.0- 45.0	40.0- 45.0		
K2. reading	Mean± SD	43.70±1.78	43.25±1.71	Z_{MWU}= 0.740	0.459
	Median (IQR)	43.0 (42.0- 45.0)	43.0 (42.50- 43.50)		
	Range	41.0- 47.0	41.0- 47.0		
BCVA	Mean± SD	0.75± 0.26	0.89± 0.14	Z_{MWU}= 1.61	0.107
	Median (IQR)	0.80 (0.70- 1.0)	1.0 (0.70- 1.0)		
	Range	0.20- 1.0	0.70- 1.0		

P value< 0.05 is significant, P value< 0.01 is highly significant SD: Standard deviation, IQR: Interquartile range, BCVA: Beast corrected visual acuity,* Z_{MWU} *= Mann- Whitney U test,

There was no statistically significant difference between the two groups regarding visual acuity, sphere and cylinder before treatment (P > 0.05). Also, there was no statistically significant difference between the two groups regarding K reading and BCVA before treatment (P > 0.05).

Table (4): Comparison of the pterygium size and time of surgery between group 1 and groups 2.

Variable		Group 1 (N=20)	Group 2 (N=20)	Test value	P-value
Ptergium extent over cornea (mm)	**Mean± SD**	1.60± 0.50	1.55± 0.51	Z_{MWU}= 0.316	0.799
	Median (IQR)	2.0 (1.0- 2)	2.0 (1.0- 2.0)		
	Range	1.0- 2.0	1.0- 2.0		
Time of surgery (min.)	**Mean± SD**	20.0± 3.49	5.20± 1.01	Z_{MWU}= 5.45	**<0.001**
	Median (IQR)	20.0 (18.5- 22.5)	5.0 (4.5- 6.0)		
	Range	12.0- 25.0	4.0- 7.0		

P value< 0.05 is significant, P value< 0.01 is highly significant SD: Standard deviation, IQR: Interquartile range, ZMWU = Mann- Whitney U test.

On comparison of time of surgery between group 1 and group 2, group 1 had longer time of surgery than group 2 (20.0± 3.49 min. Vs 5.20± 1.01 min., p<0.001) while there were no significant differences between the two groups as regards the pterygium size (p>0.05) as shown in Table (4).

Table (5): Comparison between the studied groups regarding post-operative complications.

Variable		Group 1 (N=20)		Group 2 (N=20)		Test value	P-value
		No.	**%**	**No.**	**%**		
Discomfort after surgery	**FB sensation from stitch**	20	100.0%	0	0.0%	X^2= 40.0	**<0.001**
	No	0	0.0%	20	100.0%		
Hyperemia (1 week)	**Yes**	20	100.0%	0	0.0%	X^2= 40.0	**<0.001**
	No	0	0.0%	20	100.0%		
Hyperemia (1 month)	**Yes**	0	0.0%	2	10.0%	X^2= 0.526	0.468
	No	20	100.0%	18	90.0%		
Subconjunctival hemorrhage	**Yes**	1	5.0%	0	0.0%	X^2= 0.0	1.00
	No	19	95.0%	20	100.0%		
Corneal melting	**Yes**	0	0.0%	0	0.0%	X^2= 0.0	1.00
	No	20	100.0%	20	100.0%		

***P value< 0.05 is significant, P value< 0.01 is highly significant SD: Standard deviation, IQR: Interquartile range,* X^2= Chi- Square test.**

Regarding complication, all cases (100%) in group 1 had foreign body sensation and hyperemia for 1 week. One case experienced subconjunctival hemorrhage. In group 2, two cases experienced hyperemia for 1 month. There were significant differences between the two groups as regards discomfort after surgery and hyperemia after 1 week (p<0.001). There were no significant differences between the two groups as regards hyperemia after 1-month, subconjunctival hemorrhage, and corneal melting (p>0.05). Recurrence after one month was significantly higher in group 2 compared to group 1 (p>0.001) while there were not significantly differences between the two groups regarding recurrence after 1 week, after 3 months and after 6 months (p>0.05).

Table (6): Comparison between the studied groups regarding recurrence.

Variable		Group 1 (N=20)		Group 2 (N=20)		Test value	P-value
		No.	%	No.	%		
Recurrence after 1 week	**Yes**	0	0.0%	0	0.0%	X^2= 0.0	1.00
	No	20	100.0%	20	100.0%		
Recurrence after 1 month	**Yes**	0	0.0%	16	80.0%	X^2= 23.4	**<0.001**
	No	20	100.0%	4	20.0%		
Recurrence after 3 months	**Yes**	0	0.0%	0	0.0%	X^2= 0.0	1.00
	No	20	100.0%	20	100.0%		
Recurrence after 6 months	**Yes**	0	0.0%	4	20.0%	X^2= 2.5	0.114
	No	20	100.0%	16	80.0%		

P value< 0.05 is significant, P value< 0.01 is highly significant SD: Standard deviation, IQR: Interquartile range, **X^2= Chi- Square test.**

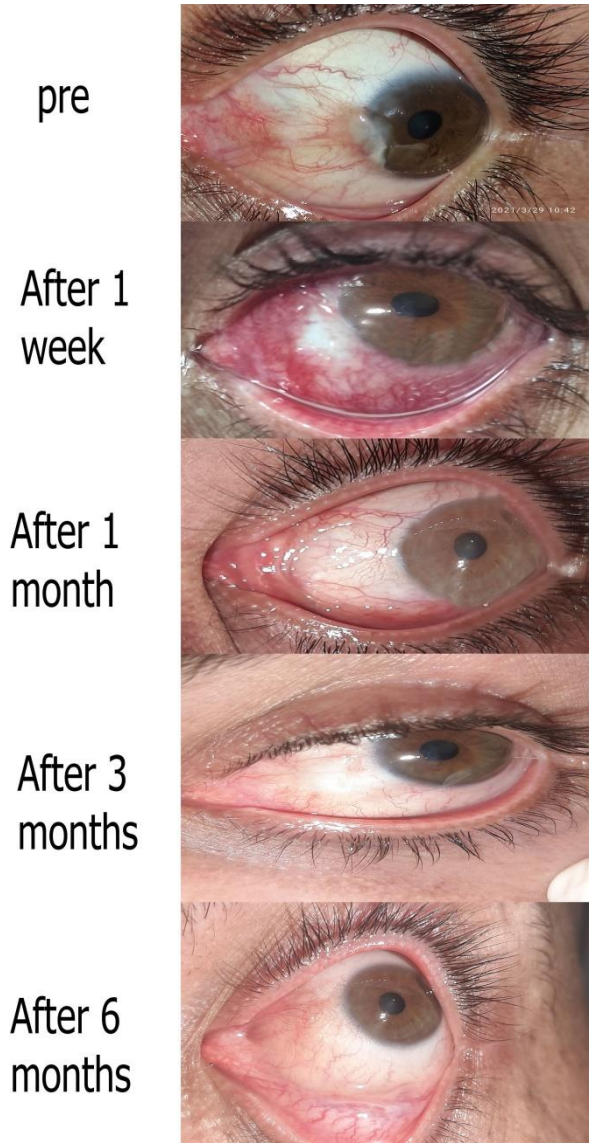

Figure (1): A case 2 G1 a case of ptergium excision with bare scelera and application of mitomycin

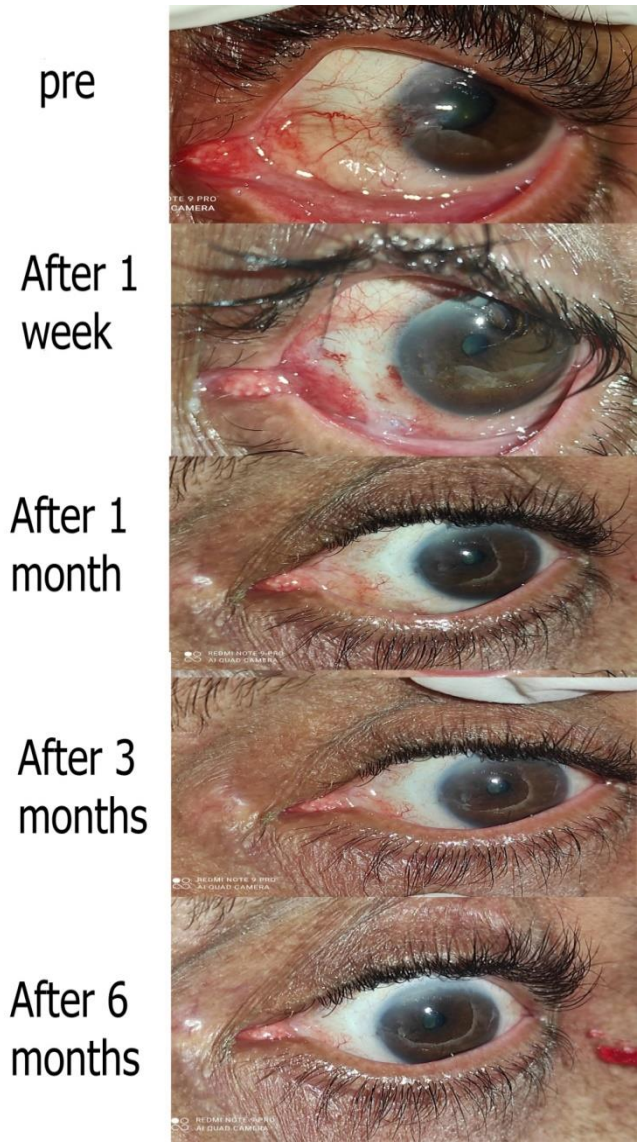

Figure (2): A case 11 G1 a case of ptergiun excision with bare scelera and application of mitomycin

Figure (3): A case 2 G2 a case of avastim injection subptergium

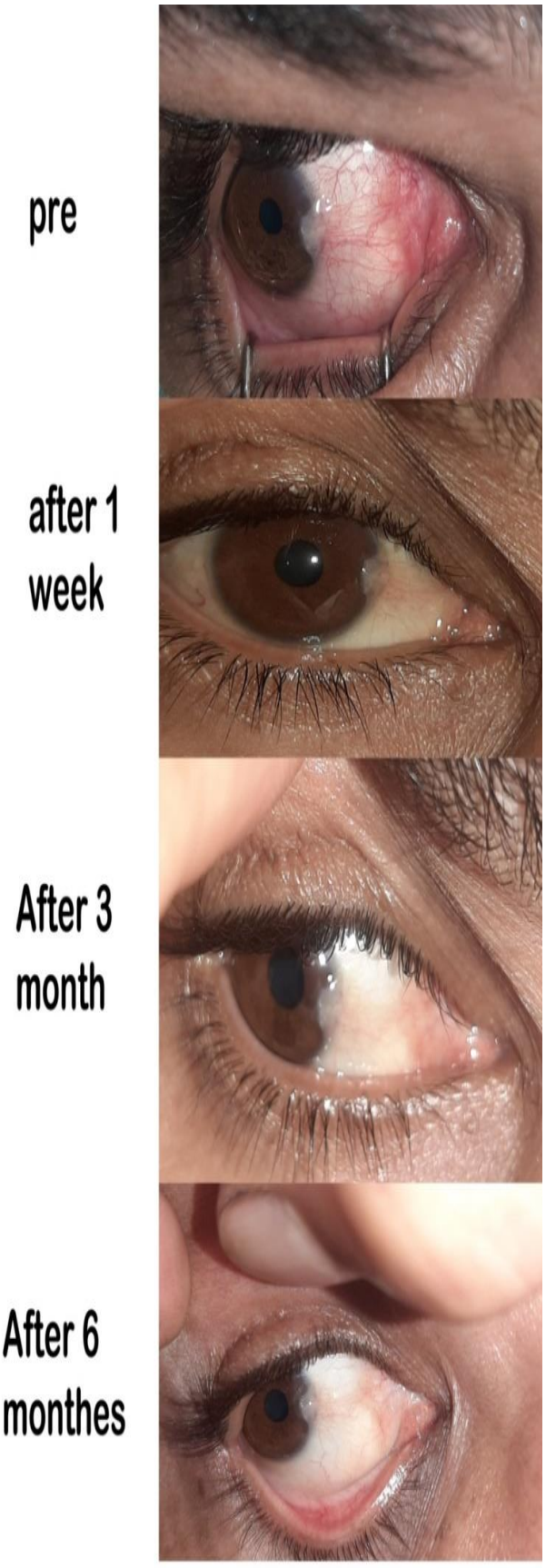

Figure (4): A case 7 G2 A case of avastin injection subptergium

Table (7): Comparison between the studied groups eye examination after treatment.

Variable		Group 1 (N=20)		Group 2 (N=20)		Test value	P-value
		No.	%	No.	%		
Difference in cylinder after surgery	Yes (-0.25)	2	10.0%	0	0.0%	X^2= 0.0	1.00
	No	18	90.0%	20	100.0%		
Difference of BCVA	Yes	0	0.0%	0	0.0%	X^2= 0.0	1.00
	No	20	100.0%	20	100.0%		
Difference of sphere	Yes	0	0.0%	0	0.0%	X^2= 0.0	1.00
	No	20	100.0%	20	100.0%		

***P value< 0.05 is significant, P value< 0.01 is highly significant SD: Standard deviation,* X^2= Chi- Square test.**

There were not significantly differences between the two groups regarding difference in cylinder, BCVA and sphere after surgery (p>0.05).

Table (8): Comparison of the cylinder between group 1 and groups 2 at different periods.

Cylinder		Group 1 (N=20)	Group 2 (N=20)	Test value	P-value
Pre-operative	Mean± SD	-1.14±0.96	-0.92±0.47	Z_{MWU}= 0.553	0.580
	Median (IQR)	-1.0 (-1.50- -0.50)	-1.0 (-1.0- -0.50)		
	Range	-3.25- (0.75)	-2.0- (-0.25)		
After 1 month	Mean± SD	-0.79±0.40	-0.75±0.40	Z_{MWU}= 0.479	0.632
	Median (IQR)	-0.75 (-1.0 – -0.50)	-0.75 (-0.75 – -0.50)		
	Range	-1.75 – -0.25	-1.75 – -0.25		
After 3 months	Mean± SD	-0.67± 0.33	-0.66± 0.33	Z_{MWU}= 0.096	0.924
	Median (IQR)	-0.72 (-0.95 – -0.40)	-0.74 (-0.65 – -0.50)		
	Range	-1.60- – -0.25	-1.63 – -0.25		
After 6 months	Mean± SD	-0.73± 0.30	-0.74± 0.40	Z_{MWU}= 0.089	0.929
	Median (IQR)	-0.74 (-1.0 – -0.50)	-0.73 (-0.75 – -0.50)		
	Range	-1.75 – -0.25	-1.75 – -0.25		

P value< 0.05 is significant, P value< 0.01 is highly significant SD: Standard deviation, IQR: Interquartile range, ZMWU = Mann- Whitney U test.

On comparison of cylinder between group 1 and group 2. There were no significant differences between the two groups as regards the cylinder after 1, 3 and 6 months (p>0.05) as shown in Table (8).

There were no significant differences between cylinder after 6 months compared to that after 1 months in both group 1 and group 2.

Table (9): Comparison of the BCVA between group 1 and groups 2 at different periods.

BCVA		Group 1 (N=20)	Group 2 (N=20)	Test value	P-value
Pre-operative	Mean± SD	0.75± 0.26	0.89± 0.14	Z_{MWU}= 1.61	0.107
	Median (IQR)	0.80 (0.70- 1.0)	1.0 (0.70- 1.0)		
	Range	0.20- 1.0	0.70- 1.0		
After 1 month	Mean± SD	0.86±0.12	0.88±0.13	Z_{MWU}= 0.506	0.616
	Median (IQR)	0.80 (0.80- 1.0)	0.82 (0.80- 1.0)		
	Range	0.70- 1.00	0.70- 1.00		
After 3 months	Mean± SD	0.88±0.10	0.89±0.10	Z_{MWU}= 0.316	0.754
	Median (IQR)	0.82 (0.81- 1.0)	0.83 (0.80- 1.0)		
	Range	0.70- 1.00	0.71- 1.00		
After 6 months	Mean± SD	0.87±0.07	0.88±0.17	Z_{MWU}= 0.243	0.809
	Median (IQR)	0.81 (0.80- 1.0)	0.82 (0.80- 1.0)		
	Range	0.72 - 1.00	0.70- 1.00		

P value< 0.05 is significant, P value< 0.01 is highly significant SD: Standard deviation, IQR: Interquartile range, ZMWU = Mann- Whitney U test.

On comparison of BCVA between group 1 and group 2. There were no significant differences between the two groups as regards the BCVA after 1, 3 and 6 months (p>0.05) as shown in table (9). There were no significant differences between BCVA after 6 months compared to that after 1 months in both group 1 and group 2.

5. Discussion

This cross-sectional study was conducted in Ophthalmology department of Al-Zahraa University Hospital. This study was conducted on 40 patients who had pterygium. They classified randomly into: Group 1 (G1): Included 20 patients who underwent application of mitomycin C after pterygium surgical excision. Group 2 (G2): Included 20 patients who underwent anti-VEGF sub pterygium injection without excision.

The main results of this study were to discuss the benefits and outcomes for the patient as following:

Regarding side, there are 10 (50%) located at left side and 10 (50%) located at right side in group 1, while group 2, 8 (40%) were in left side and 12 (60%) at right side with no statistically significant difference between the two groups (P > 0.05). Also, there was no statistically significant difference regarding between the two groups State of ptergyuim (P > 0.05) as there was 40% were membranous, 30% fleshy and 30% moderate in group 1 while in group 2, there was 50% were membranous, 30% fleshy and 20% moderate. Also, there no statistically significant difference between the two groups regarding pre-operative examination. This was in line with the study by Nassar et al., [6] who reported that the two studied groups were statistically comparable as regard main complain and the Side of pterygium in addition to the pre-treatment eye examinations. Also, in agreement with our results the study by Hwang and Choi, [7] **reported** that there was no statistically significant difference between the studied groups regarding laterality, preoperative pterygium grade, or horizontal distance from the corneal limbus to the pterygium head among the groups. Also, there was

no statistically significant difference between the studied groups regarding Horizontal pterygium size. In agreement with our results Kocabora et al., [8] reported that both groups were comparable regarding the preoperative criteria.

Regarding the postoperative complications among the studied groups, we found that all cases (100%) in group 1 had foreign body sensation and hyperemia for 1 week. One case experienced subconjunctival hemorrhage. In group 2, two cases experienced hyperemia for 1 month. There were significant differences between the two groups as regards discomfort after surgery and hyperemia after 1 week ($p<0.001$). There were no significant differences between the two groups as regards hyperemia after 1-month, subconjunctival hemorrhage, and corneal melting ($p>0.05$).

Agree to us most studies concluded that anti-VEGF is safe and has no systemic complications were detected Kocabora et al., [8].

The study by Narsani et al., [9] stated that, there were no complications observed in (MMC) group which vary according to the concentration and the duration of application. With the most commonly used dose of 0.02% for 2 minutes, there were no severe complications detected.

Also, Hwang and Choi, [7] reported that during the follow-up period, subconjunctival hemorrhage occurred in two eyes in the control group, one eye in the mitomycin C group, and two eyes in the bevacizumab group. All patients completely recovered, and no other abnormal ocular or systemic complications were observed during the six-month follow-up period. There was no significant difference in preoperative and postoperative corneal endothelial cell densities.

Agree with us, Albialy and Al-Nashar [10], reported that Subconjunctival hemorrhage on the first postoperative day was reported in three (10%) eyes in group A, five (16.6%) eyes in group B and six (20%) eyes in group C ($P=0.24$). In MMC group, no other significant complications were reported such as scleral thinning or necrosis throughout the follow-up period. In addition, the normal nasal conjunctiva in the region where bevacizumab was injected did not show any ischemic changes or necrosis during the follow-up period.

Agree to us, in the systematic review and Meta-Analysis of Randomized Controlled Trials by Sun et al., [4], 1045 eyes in 18 randomized controlled trials (RCTs) enrolled, 17 studies reporting complications were analyzed. There was no statistically significant difference between bevacizumab group and control group (RR 0.87, 95% CI 0.66–1.13, $P = 0.30$; Pheterogeneity = 0.52, $I2 = 0\%$) (supplementary data file). Further analysis of the subconjunctival hemorrhage rate showed that a statistically significant difference was not found between groups (RR 1.50, 95% CI 0.63–3.59, $P = 0.36$; Pheterogeneity = 0.69, $I2 = 0\%$). Regarding recurrence among the studied groups, our results showed that after one month was significantly higher in group 2 compared to group 1 ($p>0.001$) while there were not significantly differences between the two groups regarding recurrence after 1 week, after 3 months and after 6 months ($p>0.05$).

Disagree to us, the study by Nassar et al., [6], reported that the pterygium recurred in 7 cases (35%) out of 20 cases. The recurrence in bevacizumab group occurred in 6 cases (60%) out of 10 cases. In MM-C group the recurrence occurred in one case

(10%) out of 10 cases, with statistical significance.

Disagree to us, the study by Hwang and Choi, [7], **reported** that No recurrence was observed at one day, one week, or one month after surgery. However, at three months, recurrence was observed in eight eyes (24.2%) in the control group, one eye (3.4%) in the mitomycin C group, two eyes (5.6%) in the bevacizumab group. All treatment groups showed significantly lower recurrence rates compared to the control group but did not differ from each other. At six months, recurrence was observed in 15 eyes (45.5%) in the control group, three eyes (10.3%) in the mitomycin C group, and 15 eyes (41.7%) in the bevacizumab group. Similarly, as the recurrence rate at six months differed significantly in all groups (p = 0.004), found that the mitomycin C groups had significantly lower recurrence rates compared to the control and bevacizumab groups. Recurrence rate did not differ between the control and bevacizumab groups.

Disagree to us, Albialy and Al-Nashar, [10], reported that Recurrence of pterygium was recorded during the 6-month follow-up period, where two (6.7%) eyes in group A, two (6.7%) eyes in group B, and 11 (36.7%) eyes in group C had recurrence by the end of the follow-up period, with a statistically significant difference (P=0.01).

This variability of the recurrence rate between studies may be due to differences in definition of recurrence, surgical technique, experience, patient demographics, racial and environmental factors.

Comparison between the studied groups eye examination after treatment revealed that There were not significantly differences between the two groups regarding difference in cylinder, BCVA and sphere after surgery and after 1, 3 and 6 months ((p>0.05).

Our results were supported by Albialy and Al-Nashar, [10] who reported that the changes in keratometry and corneal astigmatism showed no statistically significant differences between the two groups of MMC and Avastin injection; however, there was a significant difference with bare scleral technique group (P=0.001).

In disagreement with our results the study by Singh et al., [11] reported that There was no significant change in BCVA, local or systemic adverse effects observed during 8 weeks of Bevacizumab (0.05 ml, 1.25 mg) injection. However, 13 out of 20 patients (65%) developed subconjunctival haemorrhage, which resolved spontaneously after 2-3 weeks interval, can be considered as a minor complication of the procedure. Our study was supported by Nasef et al., [12] aimed to assess the role of antivascular endothelial growth factor (Avastin) in the management of primary pterygium and reported that There was a difference in visual acuity between preinjection of Avastin and 3 months postinjection by mean −0.10±0.10; 16 patients showed an improvement (53.3%), while 14 patients were stable (46.7%). There is a difference in astigmatism between preinjection of Avastin and 3 months postinjection by mean (−0.15±0.33); 10 patients showed an improvement (33.3%), while 20 patients did not show an improvement (66.7%). No increase in astigmatism occurred in any patient postinjection. There was a highly significant decrease in color intensity starting from the 2nd week till the end of the 3rd month postinjection. There was no significant change in ocular tension postinjection.

6. Conclusion

The application of mitomycin C in comparison to sub pterygium injection of Avastin without excision are safe treatments. The two method was associated with low recurrence rates, but the use of Avastin without excision is superior in terms of complications as the mitomycin C was applied after an operation all cases experienced Discomfort after Surgery and Hyperemia after 1 week. Further comparative studies with larger sample size and longer follow up are needed to confirm the current results.

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