

Outcomes of bleb needling in primary glaucoma: A prospective interventional study in a South Indian population

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Purpose: This study was conducted to assess the outcomes of bleb needling for the treatment of failure of filtration surgeries in primary glaucoma with a follow-up of six months. **Methods:** This prospective interventional study included patients with primary glaucoma who underwent trabeculectomy or combined glaucoma and cataract surgery with failed or failing bleb after six weeks of surgery and less than two years. A comprehensive examination including best-corrected visual acuity (BCVA), intraocular pressure (IOP) measurement, gonioscopy, slit-lamp examination, and bleb morphology grading was done. Selected patients underwent a subconjunctival bleb needling with mitomycin C (MMC) (dose 0.2 mg/ml). Postoperatively, patients were followed up on the first, third, and sixth months and were assessed with respect to IOP, need for antiglaucoma medication (AGM), and complications. **Results:** Sixty eyes of 59 patients were included. Preoperatively, 33.3% of patients were on one AGM, whereas postoperatively at the third month 51.7% and at the sixth month 50% of patients were on no AGM. There was a statistically significant decrease in IOP ($P < 0.001$) from preoperative (mean: 23.8 ± 7.86 mmHg) to postoperative first month (mean: 19.8 ± 9.08 mmHg), third month (mean: 17.4 ± 5.4 mmHg) and sixth month (mean 16.6 ± 4.39). According to the defined criteria in the current study, we achieved 22 (37.9%) successes, 31 qualified successes (53.4%), and 5 (8.6%) failures. Univariate regression analysis showed a higher failure rate among younger age groups. Gender, laterality, and intraoperative complications were not significant statistically. **Conclusion:** Bleb needling is a safe and effective procedure for the treatment of failed filtration surgeries.

Key words: Bleb needling, mitomycin C, trabeculectomy

Trabeculectomy is the standard surgical treatment for medically uncontrolled glaucoma. It is performed by creating a fistula in the sclera at the limbus and thereby redirecting aqueous from the anterior chamber (AC) to the subconjunctival space. Bleb scarring and fibrosis can occur as a part of wound healing response and it is one of the most common causes of filtration failure.^[1]

Bleb needling is a simple procedure to restore bleb function.^[2] The technique is to enter transconjunctivally using a 26- or 30-G needle, thereby freeing the scar tissue adherent between the conjunctiva and the sclera. This can be done in the outpatient department on a slit-lamp or in an operation theater. Antimetabolites like 5-fluorouracil (5-FU) and mitomycin C (MMC) can be used as adjunctive therapy to prevent bleb scarring and fibrosis before or after the procedure.^[3] Analysis of outcomes of bleb needling revision for the failure of filtration surgeries in primary angle-closure and primary open-angle glaucoma has not been reported in the literature from the south Indian population.

This study aims to assess the outcomes and success rates of the bleb needling technique for filtration surgery failure in

primary glaucoma in the south Indian population attending a tertiary care center with a follow-up of six months.

The primary outcome is the reduction of IOP following six months of bleb needling.

Secondary outcomes were (1) the number of medications reduced or discontinued, and (2) the assessment of complications following bleb needling.

Methods

This is a prospective, interventional study done in a tertiary care center in south India from December 2018 to January 2020.

The inclusion criteria were (1) patients aged 18 years or above; (2) patients with a diagnosis of primary open-angle glaucoma (POAG), juvenile open-angle glaucoma (JOAG), or primary angle-closure glaucoma (PACG); (3) the patient should have had a failed filter in the affected eyes after six weeks and

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less than two years of surgery; (4) eyes with IOP less than 21 mmHg that did not meet the target IOP range for the stage of glaucoma despite medical therapy.

The exclusion criteria were patients with (1) multiple trabeculectomies, (2) eyes with previous needling procedures, (3) eyes with Glaucoma drainage devices, (4) monocular status (5) all forms of secondary glaucoma including pseudoexfoliation and pigmentary glaucoma. Patients were also excluded if they were pregnant or breastfeeding.

The study was approved by the Institutional Human Ethics Committee (IHEC). The study adhered to the tenets of the Declaration of Helsinki. Written, informed consent was taken from each participant. Demographic data, date of trabeculectomy, preoperative anti-glaucoma medications (AGM), and past ocular surgeries were recorded. Best-corrected visual acuity (BCVA) was determined using standard Snellen charts. A complete slit-lamp examination of the anterior segment was done. Bleb morphology assessment was done by Indiana bleb appearance scale.^[4] Intraocular pressure (IOP) was measured by the Goldmann applanation tonometer (GAT). Gonioscopy was done using Volk 4 mirror indentation gonio lens. A detailed fundus evaluation was performed with a +90 D lens and with an indirect ophthalmoscope.

Surgical technique

Bleb needling was done in the operation theater under all aseptic precautions. After sub-tenons block anesthesia, painting and draping of the ocular adnexa was done with 10% povidone-iodine solution. A corneal traction suture was applied [Fig. 1a], and a bent 26-G needle was used to perform the sub-conjunctival needling [Fig. 1b]. The needle was entered 6–8 mm from the limbus into the bleb and adhesions were cut beneath the bleb in the subconjunctival space in an attempt to lift the scleral flap to permit egress of aqueous humor [Fig. 1c]. A subconjunctival injection of 0.2 mg/ml MMC is injected.^[5] Postoperatively, patients were given topical steroids tapered 2 weekly over three months, an antibiotic eyedrop for one month, and cycloplegics for one month.

Patients were followed up on day 1, day 15, day 30, and at 3 and 6 months. The following parameters were recorded: intraoperative and postoperative complications, reduction in preoperative AGM, BCVA using standard Snellen charts, bleb morphology grading by Indiana bleb appearance scale (at 3

and 6 months),^[4] anterior segment examination, postoperative IOP measurement, repeat gonioscopy and detailed fundus evaluation.

Statistical analysis

The demographic variables are presented with descriptive statistics. The Chi-squared test was used to find the association between categorical variables. Correlation and regression analysis was used to find the relationship between independent and dependent variables. The continuous variables at different follow-ups were compared using paired *t*-test or analysis of variance (ANOVA). A *P* value of <0.05 was considered statistically significant. All the statistical analyses was done using statistical software Jamovi version 1.6.7.

Results

Sixty eyes of 59 patients were included in the study. The mean age was 60 ± 16.5 years. Thirty-five (58.3%) eyes were diagnosed with POAG, 21 (35.0%) were diagnosed with PACG, and 4 (6.7%) were diagnosed with JOAG. The mean duration between trabeculectomy and bleb needling was 15.2 ± 9.14 months; the median was 20.5 months, with a range of 1.5–24 months. Preoperatively, the majority of patients (33.3%, 20) were on one AGM, whereas postoperatively the majority of patients in the third month (51.7%, 30) and sixth month (50%, 29) were on no AGM [Table 1].

Postoperative complications included hyphema in 2 (3.3%), subconjunctival hemorrhage in 5 (8.3%), both hyphema and subconjunctival hemorrhage in 1 (1.7%), and shallow AC in 4 (6.7%) patients. All the above complications resolved spontaneously in one month. One patient (1.7%) had serous choroidal detachment which resolved spontaneously in three

Table 1: Comparison of preoperative and postoperative AGM

AGM	Pre-needling (n=60)		1 Month (n=60)		3 Months (n=58)		6 Months (n=58)	
	n	%	n	%	No. of eyes	%	No. of eyes	%
0	16	26.7	40	66.7	30	51.7	29	50.0
1	20	33.3	15	25.0	15	25.9	15	25.9
2	14	23.3	4	6.7	11	19.0	12	20.7
3	10	16.7	1	1.7%	2	3.4	2	3.4

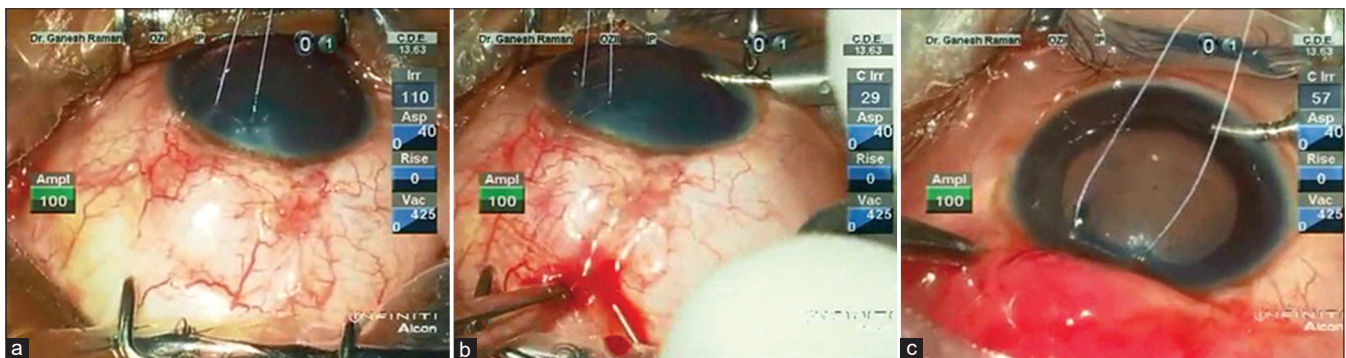


Figure 1: (a) Corneal traction suture for exposing the site of surgery, (b) A 26G needle is used for needling the bleb, (c) A diffuse bleb seen as an end point

weeks with topical and oral steroids, and 1 (1.7%) conjunctival buttonholes which required suturing postoperatively. Forty-six patients (76.7%) did not have any postoperative complications.

The mean preoperative BCVA in LogMAR was 0.14 ± 0.21 . Postoperatively, the mean visual acuity was 0.15 ± 0.21 , 0.15 ± 0.21 , 0.16 ± 0.21 at one month, three months, and six months, respectively [Table 2].

Bleb morphology distribution

Bleb morphology grading was done by the Indiana bleb appearance grading scale.^[4] Preoperatively, the majority of patients (55%, $n = 33$) had a low bleb elevation (H1), and postoperatively 41 (70.7%) patients at the third month and 41 (68.3%) patients at the sixth month had moderate bleb elevation of H2. Preoperatively, 41 patients (68.3%) had a bleb extent equal to or greater than 2 o'clock hours but less than 4 o'clock hours. There was no significant change in the extent of bleb in 42 (72.40%) patients in the third month and in 43 (71.70%) patients in the sixth month of follow-up. Preoperatively, the bleb was moderately vascular (V2) for 40% of patients ($n = 24$), and it was avascular (micro cysts of conjunctiva visible on the slit-lamp examination - V1) in 43 (74.10%) patients in the third month and for 42 patients (74.10%) in the sixth month. Seidel test was negative for all patients preoperatively and postoperatively at the third and sixth months [Table 3].

There was a significant reduction in IOP from preoperative mean IOP of 23.8 ± 7.86 mmHg ($n = 60$) to postoperative one-month mean IOP of 19.8 ± 9.08 mmHg ($n = 60$), third-month mean IOP of 17.4 ± 5.4 mmHg ($n = 58$), and sixth-month mean

IOP of 16.6 ± 4.39 mmHg ($n = 58$). The *P* value of <0.001 in all postoperative visits shows a statistically significant decrease in IOP [Table 4].

Distribution of complete success, qualified success, and failure

Complete success was defined as IOP 8 to <18 mmHg without AGM. Qualified success was defined as IOP <18 with medication and 18–21 mmHg with or without AGM. Failure was defined as IOP >21 mmHg with or without AGM.

The outcome of 22 patients (37.9%) was complete successes, of 31 patients were qualified successes (53.4%), and of 5 patients (8.6%) were considered failed. Hence a total success of 53 (91.3%) was achieved [Fig. 2]. Comparison of the complete success, qualified success, and failure groups was done by univariate analysis. There was a higher failure rate among younger age groups with a mean age of 39.2 ± 19.9 years and it was statistically significant ($P = 0.005$). The mean time difference in months from trabeculectomy to bleb needling in the complete success group was 13.6 ± 9.6 months and in the failure group was 12.1 ± 9.9 months and was not significant statistically. The mean preoperative BCVA (LogMAR) was

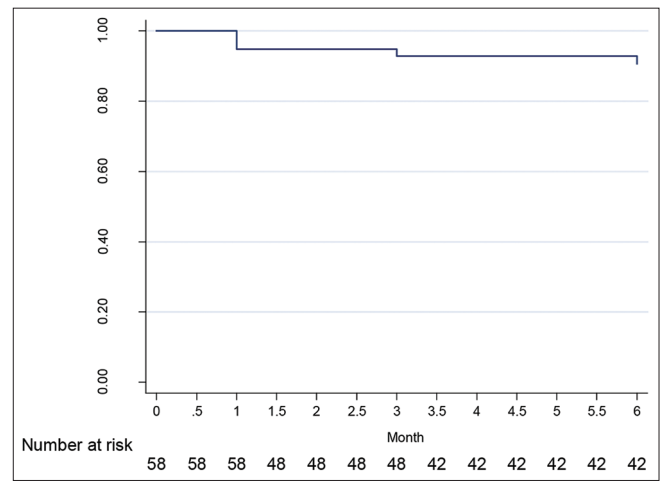


Figure 2: Kaplan–Meyer survival analysis for cumulative probability of qualified success

Table 2: Comparison of preoperative and postoperative BCVA

Best-Corrected Visual Acuity (LogMAR)			
Months	Mean	Standard Deviation	* <i>P</i>
Preoperatively ($n=60$)	0.14	0.21	
1 month ($n=60$)	0.15	0.21	0.59
3 months ($n=58$)	0.15	0.21	0.59
6 months ($n=58$)	0.16	0.22	0.18

*Wilcoxon test

Table 3: Distribution of bleb morphology based on the Indiana bleb appearance scale

Grade	Baseline ($n=60$)		3 Months ($n=58$)		6 Months ($n=58$)	
	No. of eyes	Percentage	No. of eyes	Percentage	No. of eyes	Percentage
H0	11	18.3%	0	0	0	0
H1	33	55.0%	16	27.6%	16	26.70%
H2	11	18.3%	41	70.7%	41	68.30%
H3	5	8.3%	1	1.7%	1	1.70%
E1	10	16.7%	3	5.20%	5	8.30%
E2	41	68.3%	42	72.40%	43	71.70%
E3	9	15.0%	13	22.40%	10	16.70%
V0	8	13.3%	0	0	1	1.70%
V1	21	35.0%	43	74.10%	42	70.00%
V2	24	40.0%	13	22.40%	14	23.30%
V3	7	11.7%	2	3.40%	1	1.70%
S0	60	100.0%	58	96.70%	58	96.70%

0.14 ± 0.2 for the complete success group, 0.09 ± 0.1 for the qualified success group, and 0.40 ± 0.28 for the failure group. Patients in the complete success and qualified success groups had better preoperative visual acuity than the failure group, and it was statistically significant ($P = 0.005$) [Table 5].

The mean pre-needling IOP was 24.1 ± 7.6 mmHg in the complete success group, 20.5 ± 5.3 mmHg in the qualified success group, and 29.6 ± 8.5 mmHg in the failure group. Hence pre-needling IOP was lower in the complete success group and qualified success group than in the failure group. A P value of 0.023 showed that it was statistically significant. Out of 33 POAG diagnosed patients, 1 (3%) patient had a failure; out of 21 PACG patients, 3 (14%) had a failure; and out of 4 JOAG patients, 1 (25%) had a failure. Hence there was a higher failure rate among PACG and JOAG patients. A P value of 0.03 signified that it was statistically significant. Gender, laterality, and intraoperative complications were not significant statistically. A comparison of complete success with qualified success and failure groups was done by multivariate analysis,

which showed that age and diagnosis were not statistically significant. Even though preoperative VA and IOP showed a low P value, they were not significant statistically.

Discussion

The authors conducted a prospective interventional study for assessing bleb needling for failed filtration surgery with MMC in primary glaucoma in the south Indian population in a tertiary care center with a follow-up of six months.

The mean age in our study was 60.0 ± 16.5 years. Pathak-Ray *et al.*^[6] reported the median age of 59 years (range 22–79 years)^[7] and Lee *et al.*^[5] reported the mean age of 52.1 ± 15.8 years (range 13–78 years).^[8] In the current study, 58.3% of eyes were diagnosed as POAG, 35% as PACG, and 6.7% as JOAG. Lin *et al.*^[2] reported 66% of eyes with POAG/ Normal Tension Glaucoma (NTG), 16% of eyes with chronic angle-closure, 11% of eyes with pseudo-exfoliation glaucoma, 5% of eyes with uveitic glaucoma, and 2% of eyes with pigmentary glaucoma.

Comparison between preoperative and postoperative AGM

In the current study, preoperatively, the majority of patients (33%) were on one AGM whereas postoperatively the majority of patients at the third month (51.7%) and the sixth month (50%) were on zero AGM. Patak-Ray *et al.*^[6] found that the use of AGM pre needling reduced from median 1 (range 0–4) to median 0 post needling. Lin *et al.*^[2] reported a reduction in AGM from a mean of 1.7 preoperatively to a mean of 1.2, 1.4, and 1.2 medications at 12, 24, and 36 months, respectively; this was not statistically significant.

Comparison of preoperative and postoperative bleb morphology

Preoperatively, the majority of patients had a low bleb elevation (H1) 55% (33), an extent of greater or equal to 2 o'clock hours but less than 4 o'clock hours (E2) 68.3% (n = 41),

Table 4: Comparison of preoperative and postoperative intraocular pressure (IOP)

	Mean	Standard Deviation	Median	*P(Compared with Preoperative IOP)
IOP- Preoperatively (n=60)	23.8	7.86	22.5	
IOP - 1 months (n=60)	19.8	9.08	17.5	$P < 0.001$
IOP - 3 months (n=58)	17.4	5.44	16	$P < 0.001$
IOP - 6 months (n=58)	16.6	4.39	16	$P < 0.001$

*Wilcoxon signed-rank test

Table 5: Preoperative risk factors for success and failure of bleb needling – univariate analysis

Parameters	Mean	Success n=31	Qualified success n=22	Failure n=5	P
Mean±SD ** (Min, Max)					
Age (years)	59.7±18.5 (18, 88)	65.3±8.4 (46, 77)	39.2±19.9 (18, 61)	0.005*	
Time from trabeculectomy to needling (months)	13.6±9.6 (1.5, 24)	17.5±8.2 (1.5, 24)	12.1±9.9 (1.5, 23)	0.24	
Best corrected V/A, LogMAR	0.14±0.2 (0, 0.77)	0.09±0.1 (0, 0.3)	0.40±0.28 (0, 0.77)	0.009*	
IOP - Pre needling	24.1±7.6 (12, 50)	20.5±5.3 (10, 34)	29.6±8.5 (18, 42)	0.023*	
Gender					
Female	13	8 (61.5)	3 (23.1)	2 (15.4)	0.36
Male	45	23 (51.1)	19 (42.2)	3 (6.7)	
Laterality					
Left eye	24	13 (54.2)	10 (41.7)	1 (4.2)	0.58
Right eye	34	18 (52.9)	12 (35.3)	4 (11.8)	
Diagnosis					
POAG	33	22 (66.7)	10 (30.3)	1 (3.0)	0.03*
PACG	21	6 (28.6)	12 (57.1)	3 (14.3)	
JOAG	4	3 (75.0)	0 (0.0)	1 (25.0)	
Intraoperative Complications					
Nil	46	27 (58.7)	17 (37.0)	2 (4.3)	0.41
Complication present	14	8 (57.1)	4 (28.6)	2 (14.3)	

* Chi-squared test, a P -value of <0.05 was considered statistically significant. ** ANOVA to test the significance of results

bleb was moderately vascular (V2) 40% (n = 24), Seidel's test was negative (S0) in all patients. Postoperatively at 6 months, the majority of patients had achieved a moderate bleb elevation (H2) 68.30% (n = 41), an extent of greater or equal to 2 clock hours but less than 4 clock hours (E2) 71.70% (n = 43), bleb was avascular (V1) 70% (n = 42), Seidel's was negative (S0). Histopathological studies have shown that early failed blebs have more inflammatory cells and fibroblastic activity,^[7] whereas late failed blebs have thick, well-arranged acellular collagen walls.^[7,8] No other needling study in the literature has compared preoperative and postoperative bleb morphology by the Indiana bleb appearance scale.

Comparison of preoperative IOP to postoperative IOP at 1st month, 3rd month, and 6th month

In this study, there was a significant reduction in IOP from preoperative mean IOP of 23.8 ± 7.86 mmHg to postoperative first-month mean IOP of 19.8 ± 9.08 mmHg, third-month mean IOP of 17.4 ± 5.4 mmHg, and sixth-month mean IOP of 16.6 ± 4.39 mmHg. It was statistically significant ($P < 0.001$). Pathak-Ray *et al.*^[6] found that median IOP pre needling was 24 mmHg and post needling was 14 mmHg at last follow-up ($P < 0.0001$). Lin *et al.*^[2] found that the mean pre-needling IOP was 19.8 mmHg compared to the mean post-needling IOP of 13.9 mmHg, representing an IOP reduction of 29.5%. In the study by Tsai *et al.*,^[9] the mean pre-needling IOP was 20.7 mmHg compared to post-needling IOP of 13.9 mmHg at the last follow-up ($P < 0.001$).

Distribution of complete success, qualified success, and failure

There were 22 (37.9%) successes, 31 qualified successes (53.4%), and 5 (8.6%) failures in our study. Hence, we achieved a total success in 53 (91.3%) patients. Pathak-Ray *et al.*^[6] reported complete success in 28 eyes (71.8%) and qualified success in 5 eyes (12.8%) (the above criteria with AGM). Total success was 84.6%. Shin *et al.*^[10] defined success as target IOP control with not more than two AGMs, with no repeat needling or other surgical interventions. The total success rate of the 5-FU augmented needling was 45%, 33%, and 28% in the first year, second year, and the fourth years. Pre-needling IOP >30 mmHg was a risk factor for failure and it was statistically significant ($P < 0.0003$).

Risk factors for complete success, qualified success, and failure of bleb needling.

We compared the complete success, qualified success, and failure groups by univariate analysis.

There was a higher failure rate in patients of younger age with a mean of 39.2 ± 19.9 years ($P < 0.005$). The mean preoperative BCVA (LogMAR) was 0.14 ± 0.2 for the complete success group, 0.09 ± 0.1 for the qualified success group, and 0.40 ± 0.28 for the failure group. A P value of 0.009 shows that it was statistically significant. The mean pre-needling IOP was 24.1 ± 7.6 mmHg in the complete success group, 20.5 ± 5.3 mmHg in the qualified success group, and 29.6 ± 8.5 mmHg in the failure group. Hence pre-needling IOP was lower in the complete success group and qualified success group than the failure group ($P < 0.023$).

Out of 33 patients with POAG, 1 (3%) had a failure; out of 21 PACG patients, 3 (14%) had a failure; and out of 4 JOAG patients, 1 (25%) had a failure. Hence there was a higher failure

rate among PACG and JOAG patients. A P value of 0.03 signifies that it was statistically significant. Gender, laterality, and intraoperative complications were not significant statistically.

A comparison of complete success with qualified success and failure groups was done by multivariate analysis, which showed that age, diagnosis, preoperative intraocular pressure, and baseline visual acuity were not statistically significant.

Limitation

Short follow-up was one of the important limitations of the study. A larger sample size could have highlighted important factors predisposing to failure in the multivariable analysis.

Conclusion

This study suggests that bleb needling is a safe and effective procedure for achieving a reduction in IOP in eyes with trabeculectomy failure for the initial six months. There was also a significant reduction in the number of AGM used. In six months, the authors could achieve a qualified success of 91.3%. Patients in the younger age group and with higher preoperative IOP may have more likelihood of failure although clinically relevant but was not statistically significant. Patients with these risk features should be counseled regarding the likelihood of requiring further intervention following a bleb needling.

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Conflicts of interest

There are no conflicts of interest.

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