

# Efficacy of Two Drugs in Trabeculectomy: A Quasi Experimental Study

Qirat Qurban,<sup>1\*</sup> Zeeshan Kamil,<sup>1</sup> Khalid Mahmood<sup>1</sup>

## ABSTRACT

**Objective** To find the additive effect of bevacizumab on outcome of trabeculectomy surgery augmented with mitomycin C in patients with primary open angle glaucoma on maximum topical anti glaucoma drug therapy.

**Study design** Quasi experimental study.

**Place & Duration of study** Department of Ophthalmology, Khalid Eye Clinic Karachi, from July 2018 to June 2019.

**Methodology** This study recruited 56 patients between the ages of 25 year to 50 year of both gender, divided into two groups of 28 patients each. Patients with primary open angle glaucoma with intraocular pressure (IOP) of more than 26 mmHg on maximum topical drug therapy were included. Patients of both the groups underwent traditional trabeculectomy surgery with peroperative application of mitomycin C over the scleral flap region. Patients of group A received sub conjunctival injection of bevacizumab whereas group B patients received placebo containing normal saline sub-conjunctival injection at the end of the surgery. Main outcome measures were control of intraocular pressure at the end of one year, reduction in use of topical drug therapy and vascularization of bleb. All the patients were followed up for one year. Paired t test and Chi square test were applied for statistical analysis.

**Results** Mean preoperative intraocular pressure in group A was  $28.6 \pm 1.33$  mmHg whereas in group B  $28.4 \pm 1.31$  mmHg ( $p=0.607$ ). Mean postoperative intraocular pressure in group A was  $13.0 \pm 1.29$  mmHg whereas in group B  $17.4 \pm 1.4$  mmHg. In group A 24 (85%) patients did not require any anti-glaucoma topical therapy postoperatively, and 24 (15%) patients required single drug therapy. In group B, 18 (64%) patients did not need any topical anti-glaucoma drug whereas 10 (36%) patients required single drug therapy ( $p=0.061$ ). Mild vascularization of the bleb was observed in one (0.03%) patient of group A and seven (25%) of group B ( $p=0.026$ ).

**Conclusion** Augmented trabeculectomy surgery with mitomycin C is effective in controlling the intraocular pressure but the adjuvant use of bevacizumab had an additional effect on the outcome of trabeculectomy surgery.

**Key words** Bevacizumab, Mitomycin C, Primary open angle glaucoma, Trabeculectomy.

<sup>1</sup> Khalid Eye Clinic Karachi.

## Correspondence:

Dr. Qirat Qurban<sup>1\*</sup>  
Khalid Eye Clinic,  
Karachi  
Email: qirat\_89@hotmail.com

## INTRODUCTION:

The standard surgical intervention for the reduction of uncontrolled intraocular pressure (IOP) in patients on maximal topical anti glaucoma drug therapy is trabeculectomy.<sup>1</sup> The formation of scleral flap and overlying conjunctival bleb in trabeculectomy may end up in scar tissue formation leading to subsequent elevation of the intraocular pressure and progression of glaucoma. A proliferative stage ensues after the

acute inflammatory stage is over, which lasts for a period two weeks following trabeculectomy surgery, during which re epithelialization along with new vessel and granulation tissue development form the vital components leading to failure of the bleb.<sup>2</sup> For the continuing success of trabeculectomy surgery, modulation of wound healing process is essential.<sup>3</sup>

A single peroperative application of mitomycin C (MMC) during trabeculectomy surgery is used widely since it alters the wound healing process by limiting the proliferation of fibroblasts as well as growth and replication of the endothelial cells leading to deterrence of formation of scar tissue ensuring survival of the filtering bleb. However, owing to its non specificity, the use of MMC is reported to cause potential vision threatening adverse effects such as damage to the cells, leakage from the bleb, hypotony, scarring of the cornea and endophthalmitis.<sup>3-5</sup> This necessitates the use of an adjunctive treatment modality which is safe, effective and restricts the formation of scar tissue formation together with minimal vision threatening adverse effects, thus, enhancing the success rate of trabeculectomy surgery.

The presence of vascular endothelial growth factor (VEGF) has been found in diverse ocular pathologies and is being studied thoroughly.<sup>6-8</sup> It is known for its part in the healing process and its levels are found to be elevated after surgery for about four weeks. Also, elevated VEGF levels are found within the aqueous humour of patients suffering from primary open angle glaucoma (POAG).<sup>6</sup> Bevacizumab (anti-VEGF), is a humanized monoclonal antibody which adheres to as well as blocks the biological action of all the subtypes of VEGF together with anti-proliferative and anti-fibroblastic characteristics.<sup>9</sup> Based upon the aforementioned information this study aimed at observing the additional effect of using sub conjunctival bevacizumab injection as an adjuvant modality in mitomycin C enhanced trabeculectomy surgery in patients with primary open angle glaucoma.

**METHODOLOGY:**

This quasi experimental study was carried out at Khalid Eye Clinic Karachi, from July 2018 to June 2019 on 56 patients between the ages of 25 year to 50 year of both gender. The patients were divided

into two groups of 28 each. All patients were briefed about the study protocol and approval was obtained from the ethical review committee. Informed consent was obtained. Patients of POAG, visual field test and optic disc changes pertaining to POAG, intraocular pressure of more than 26 mmHg on maximum topical drug therapy were included. Patients of any other type of glaucoma, history of ocular trauma or surgery, active allergy, infection, or inflammatory disease at the ocular surface, systemic disease affecting the ocular surface, need for combined phaco-trabeculectomy, prior intraocular surgery except for uncomplicated phacoemulsification and history of contraindication to bevacizumab use, were excluded.

A systematic ocular and systemic history was taken and complete eye examination was done preceding the operation comprising of best corrected visual acuity, corneal pachymetry, slit lamp examination, gonioscopy, Goldmann applanation tonometry, optic disc and fundus examination. Patients of both the groups underwent traditional trabeculectomy surgery with peroperative application of mitomycin C over the scleral flap region. Patients of group A received a single intraoperative sub conjunctival injection of 1.25 mg in 0.05 ml bevacizumab near the bleb upon completion of the trabeculectomy surgery whereas group B patients received a placebo sub conjunctival injection containing normal saline at the end of the surgery. Main outcome measures were control of intraocular pressure, reduction in topical drug therapy use and vascularization of bleb. All the patients were followed up for a period of one year. Paired t test and Chi square test were applied for statistical analysis. SPSS version 25.0 was used to tabulate data and p value <0.05 taken as significant.

**RESULTS:**

The mean age of the patients was 38.5±8.57 year. There were thirty four (61%) females and twenty two (39%) males. Right eye was involved in 37 (66%) patients and left eye in 19 (34%). Mean preoperative intraocular pressure in group A was 28.6±1.33 mmHg whereas in group B 28.4±1.31 mmHg (p=0.607) (Table 1). Mean postoperative intraocular pressure in group A was 13.0±1.29 mmHg and in group B 17.4±1.4 mmHg (p=0.000) by paired t test. In group A 24 (85%) patients did not require any anti-glaucoma topical therapy postoperatively,

**Table 1: Pre and Post Operative IOP Among The Two Groups**

Groups	Mean preoperative IOP	Mean postoperative IOP
Group A	28.6±1.33 mmHg	13.0±1.29mmHg
Group B	28.4±1.31 mmHg	17.4±1.4 mmHg

whereas 4 (15%) required single drug therapy.

In group B, 18 (64%) patients did not need any topical anti-glaucoma drug whereas 10 (36%) required single drug therapy ( $p=0.061$ ). Mild vascularization of the bleb was observed in 1 (0.03%) patient of group A and 7 (25%) of group B ( $p=0.026$ ). Complications such as scleral thinning, blebitis or endophthalmitis were not observed in any patient of either group. Mean follow up period was  $372.4 \pm 6.8$  days.

#### DISCUSSION:

Trabeculectomy is the conventional treatment for the management of refractory glaucoma. Often times, subsequent to the initial control of intraocular pressure, the healing process and scar tissue formation at the site of scleral flap and bleb construction leads to failure of IOP control.<sup>10,11</sup> Migration and proliferation of the fibroblasts play a pivotal role in impeding the aqueous flow via the scleral tunnel post trabeculectomy owing to the increased inflammatory activity.<sup>12</sup> The development of angiogenesis also forms an essential component of the wound healing process. Some chief angiogenic factors comprise of vascular endothelial growth factor, basic fibroblast growth factor, insulin like growth factor and epithelial growth factor.<sup>2</sup> Various methods have been tried to effectively alter the scar tissue formation post trabeculectomy, such as the widespread use of anti-scarring agent, mitomycin C (MMC), to enhance the trabeculectomy surgery outcome by averting fibrosis and failure of trabeculectomy but it has noteworthy adverse effects and complications on the ocular tissues.<sup>13,14</sup>

It has been found that vascular endothelial growth factor is present in elevated quantities in the aqueous humor in patients of primary open angle glaucoma after the trabeculectomy surgery.<sup>3,15</sup> The utilization of an anti VEGF agent can cause a noticeable reduction in the VEGF levels along with influencing the formation of scar tissue and wound healing by plummeting the levels of released cytokines from the vessels of wound site by inhibiting angiogenesis.<sup>6,16</sup> Anti VEGF agent (bevacizumab) due to its direct modulation of fibroblast activity, circuitously makes the scleral flap less adherent to the original wound site.<sup>1,17</sup>

With this understanding, sub conjunctival bevacizumab injection was applied peroperatively in this study together with mitomycin C to observe the additional effect in lowering the intraocular pressure effectively. The sub conjunctival route of administration of bevacizumab was preferred

because of the long biological half life via this route, fastening to the scleral matrix and enhanced storage.<sup>18</sup> Kahook et al was the first to document the potential use of anti VEGF agents for modulation of the wound.<sup>19</sup> Cornish et al reported peroperative utilization of single intravitreal bevacizumab injection as an adjunct in trabeculectomy surgery averting the need for topical anti glaucoma therapy at six months.<sup>20</sup> Vandewalle et al applied single intra cameral injection of bevacizumab at the end of trabeculectomy surgery and found an increased success rates with a decreased need for postoperative intervention to maintain the target IOP.<sup>21</sup>

Zarei et al investigated the safety and synergistic consequence of using topical bevacizumab after trabeculectomy surgery together with MMC and found no significant affect on the IOP trend.<sup>22</sup> In the present study bevacizumab was injected sub conjunctivally near the bleb preoperatively and by the end of one year follow up period there was a significant additional reduction in the intraocular pressures of patients of group A. A study by Kaushik et al compared the effectiveness of adjunctive bevacizumab over MMC modulated trabeculectomy surgery in patients with primary open angle glaucoma and found that adjunctive bevacizumab was effective and equivalent to MMC for IOP control.<sup>23</sup> No complications like scleral thinning, blebitis or endophthalmitis were observed in any patient of either group in the present study.

#### CONCLUSION:

Mitomycin enhanced trabeculectomy surgery is effective in controlling the intraocular pressure in patients of primary open angle glaucoma but the adjunctive use of sub conjunctival bevacizumab injection has an additional effect on the final outcome with regards to IOP control, vascularization and need for postoperative topical anti glaucoma therapy.

#### REFERENCES:

1. Nilforushan N, Yadgari M, Kish SK, Nassiri N. Subconjunctival bevacizumab versus mitomycin C adjunctive to trabeculectomy. *Am J Ophthalmol.* 2012;153:e352-e7.
2. Grewal DS, Jain R, Kumar H, Grewal SP. Evaluation of subconjunctival bevacizumab as an adjunct to trabeculectomy a pilot study. *Ophthalmology.* 2008;115:e2141-e5.
3. Seibold LK, Sherwood MB, Kahook MY. Wound modulation after filtration surgery.

- Surv Ophthalmol. 2012;57:530-50.
4. Wang D, Jampel HD. Imprecision medicine: The use of mitomycin c in trabeculectomy surgery. *Ophthalmol Glaucoma*. 2018;1: 149-51.
5. Jongsareejit B, Tomidokoro A, Mimura T, Tomita G, Shirato S, Araie M. Efficacy and complications after trabeculectomy with mitomycin C in normal-tension glaucoma. *Jpn J Ophthalmol*. 2005;49:223-7. doi:10.1007/s10384-004-0181-9
6. Hu DN, Ritch R, Liebmann J, Liu Y, Cheng B, Hu MS. Vascular endothelial growth factor is increased in aqueous humor of glaucomatous eyes. *J Glaucoma*. 2002;11:406-10.
7. Collete L, Larson T, Bakri S. Bevacizumab for ophthalmic disease; retina. *US Ophthalmic Rev*. 2008;2:20-4.
8. Zarnowski T, Tulidowicz-Bielak M. Topical bevacizumab is efficacious in the early bleb failure after trabeculectomy. *Acta Ophthalmologica*. 2011;89:e605-e6.
9. Iliev M, Domig D, Wolf-Schnurrbursch U, Wolf S, Sarra G. Intravitreal bevacizumab (Avastin) in the treatment of neovascular glaucoma. *Am J Ophthalmol*. 2006;142:1054-6.
10. Agarwal HC, Sharma TK, Sihota R, Gulati V. Cumulative effect of risk factors on short-term surgical success of mitomycin augmented trabeculectomy. *J Postgrad Med*. 2002;48:92-6.
11. Broadway DC, Chang LP. Trabeculectomy, risk factors for failure and the preoperative state of the conjunctiva. *J Glaucoma*. 2001;10:237-49.
12. Mietz H, Raschka B, Krieglstein GK. Risk factors for failures of trabeculectomies performed without antimetabolites. *Br J Ophthalmol*. 1999;83:814-21.
13. Singh K, Mehta K, Shaikh NM, Tsai JC, Moster MR, Budenz DL, et al. Trabeculectomy with intraoperative mitomycin C versus 5-fluorouracil. Prospective randomized clinical trial. *Ophthalmology*. 2000;107:2305-9.
14. Georgoulas S, Dahlmann-Noor A, Brocchini S, Khaw PT. Modulation of wound healing during and after glaucoma surgery. *Prog Brain Res*. 2008;173:237-e54.
15. Skuta GL, Parrish RK II. Wound healing in glaucoma filtering surgery. *Surv Ophthalmol*. 1987;32:149-70.
16. Li Z, Van Bergen T, Van de Veire S, Van de Vel I, Moreau H, Dewerchin M, et al. Inhibition of vascular endothelial growth factor reduces scar formation after glaucoma filtration surgery. *Invest Ophthalmol Vis Sci*. 2009;50:5217-5.
17. Budenz DL, Taba KE, Feuer WJ, Eliezer R, Cousins S, Henderer J, et al. Surgical management of secondary glaucoma after pars plana vitrectomy and silicone oil injection for complex retinal detachment. *Ophthalmology*. 2001;108:1628-32.
18. Nomoto H, Shiraga F, Kuno N, Kimura E, Fujii S, Shinomiya K, et al. Pharmacokinetics of bevacizumab after topical, subconjunctival, and intravitreal administration in rabbits. *Invest Ophthalmol Vis Sci*. 2009;50:4807-13.
19. Kahook MY, Schuman JS, Noecker RJ. Needle bleb revision of encapsulated filtering bleb with bevacizumab. *Ophthalmic Surg Lasers Imaging*. 2006;37:148-50.
20. Cornish KS, Ramamurthi S, Saidkasimova S, Ramaesh K. Intravitreal bevacizumab and augmented trabeculectomy for neovascular glaucoma in young diabetic patients. *Eye (Lond)*. 2009;23:979-81.
21. Vandewalle E, Zeyen T, Bergen TV, L, Spileers W, Stalmans I. One year results of intracameral bevacizumab as an adjunct to trabeculectomy in open angle glaucoma patients. *Invest Ophthalmol Vis Sci*. 2013;54:2137
22. Zarei R, Masoumpour M, Moghimi S, Fakhraei G, Eslami Y, Mohammadi M. Evaluation of topical bevacizumab as an adjunct to mitomycin C augmented trabeculectomy. *J Curr*

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91.16/j.joco.2016.10.003

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23. Kaushik J, Parihar JK, Jain VK, Gupta S, Nath P, Durgapal P, et al. Efficacy of bevacizumab compared to mitomycin c modulated trabeculectomy in primary open angle glaucoma: a one-year prospective randomized controlled study. *Curr Eye Res.* 2 0 1 7 ; 4 2 : 2 1 7 - 2 4 . doi:10.3109/02713683.2016.1164188

Author's Contributions:

Qirat Qurban: Manuscript writing & data analysis  
Zeeshan Kamil: Concept and design, data analysis & proof reading

Khalid Mahmood: Data collection & proof reading  
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