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The effect of Subconjunctival Bevacizumab as an Adjunct to Ahmed glaucoma valve implantation in eyes with Neovascular glaucoma

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ABSTRACT

Aim: to evaluate the effect of Subconjunctival Bevacizumab as an Adjunct to Ahmed glaucoma valve implantation in eyes with Neovascular glaucoma. **Method:** This is a retrospective study conducted in Irbid-Jordan at prince Rashid Bin Al Hassan military hospital between Jan. 2012 and May 2016. All patients who underwent Ahmed glaucoma valve surgery to control refractory Neovascular glaucoma were included in the study. 50 eyes were included in the study. Patients were divided into 2 groups; Group A (32 eyes) are those eyes who underwent Subconjunctival 1.25mg Bevacizumab as an Adjunct to Ahmed glaucoma valve surgery and group B (18 eyes) are those who underwent Ahmed glaucoma valve surgery without Subconjunctival Bevacizumab. Information was collected from patients regarding their age, sex, cause of NVG, number of eye drops before and after surgery, visual acuity, level of IOP before and after surgery and severity of rubeosis iridis before and after surgery. **Results:** after the use of Subconjunctival Bevacizumab the IOP level in group A was 18.1, 16.0, 13.6 and 12.9 mmHg at 1 week, 4 weeks, 3 months and 6 months respectively compared with 22.3, 21.0, 19.2 and 19.1 mmHg in group B for the same period (P value < 0.05). Also, the number of medication needed post-operatively to control IOP in group A was 3.2, 2.1, 1.1 and 0.5 at 1 week, 4 weeks, 3 months and 6 months respectively compared with 3.8, 3.0, 2.8 and 2 in group B for the same period. **Conclusion:** Subconjunctival Bevacizumab has an excellent additive effect in regression of rubeosis iridis and achievement of better intra ocular pressure control when administered at the time of Ahmed glaucoma valve surgery in patients with neovascular glaucoma and it significantly increases the success rate of the surgery.

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1. Introduction

Neovascular glaucoma (NVG) is one of the serious conditions that affect the eye because it is usually difficult to control and may lead to irreversible deterioration of vision. (1) vascular endothelial growth factor (VEGF) which is released as a result of retinal ischemia mostly caused by diabetic retinopathy or retinal vein occlusion. (2,3) VEGF will leak and reach the iris resulting in development of fibrovascular membranes and peripheral anterior synechiae at the angle that will interfere with aqueous drainage and subsequently will lead to elevation in intra ocular pressure. (4,5). Treatment options include controlling the underlying diseases, panretinal laser photocoagulation (PRP), intravitreal bevacizumab (Avastin) injection (IVA) and AVG tube surgery to control the elevation in IOP. (6) bevacizumab (Avastin) is an anti-VEGF recombinant humanized monoclonal

antibody that was initially approved for the treatment of metastatic colorectal cancer. (7) now it is widely used in ophthalmology in the management of choroidal neovascularization secondary to age related macular degeneration, diabetic macular edema, central retinal vein and NVG. bevacizumab was used in this study to evaluate its efficacy when given subconjunctivally combined with Ahmed glaucoma valve (AGV) implantation in patients with NVG.

2. Method

This is a retrospective study conducted in Irbid-Jordan at prince Rashid Bin Al Hassan military hospital between Jan. 2012 and May 2016. All patients who underwent AVG tube surgery to control refractory NVG were included in the study. Patients must also have active anterior segment neovascularization and visual acuity better than light perception with elevated intra ocular pressure (IOP) despite the use of maximum medical therapy. Patients who underwent more than one surgery for glaucoma or those who have other types of glaucoma and patients who underwent IVA before operation were also excluded from the study. All patients underwent PRP within 3 weeks before surgery.

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50 eyes were included in the study. Patients were divided into 2 groups; Group A (32 eyes) are those eyes who underwent Subconjunctival 1.25mg Bevacizumab (SCB) as an Adjunct to AVG tube surgery and group B (18 eyes) are those who underwent AVG tube surgery without SCB.

Information was collected from patients regarding their age, sex, cause of NVG, number of eye drops before and after surgery, visual acuity, level of IOP before and after surgery and severity of rubeosis iridis before and after surgery.

RESULTS

The patient's age ranged between 45 and 72 years (mean 60.5 ±8), 62% were males. There was no significant difference between the two groups regarding age and sex. The most common cause for NVG was diabetic retinopathy (65%) followed by retinal vein occlusion (29%) and uveitis (6%).

The level of IOP (in mmhg) using Goldman applanation tonometry pre and post-operatively are summarized in table 1

Table 1The level of IOP pre and post-operatively

IOP	Group A	% of reduction in IOP	Group B	% of reduction in IOP
Pre-operative	31.1	0.0%	29.9	0.0%
1 week post op.	18.1	41.8%	22.3	25.4%
4 weeks post op.	16.0	48.6%	21.0	29.8%
3 months post op.	13.6	56.3%	19.2	35.7%
6 months post op.	12.9	58.5%	19.1	36.1%

The number of medications needed to control the IOP is summarized in table 2

Table 2,The number of medications needed to control the IOP pre and post-operatively

IOP	Group A	% of reduction in No. of medications	Group B	% of reduction in No. of medications
Pre-operative	4	0.0%	4	0.0%
1 week post op.	3.2	20.0%	3.3	17.5%
4 weeks post op.	2.1	47.5%	3.0	25.0%
3 months post op.	1.1	72.5%	2.8	30.0%
6 months post op.	0.5	87.5%	2.0	50.0%

The success rate of surgery of surgery in group A was 70%, 85%, and 95% at 1,3 and 6 months respectively, while in group B the success rate was 65%, 71% and 78% at 1,3 and 6 months respectively.

There was slight insignificant drop in visual acuity post operatively in both groups at one week post operatively. The most common complication of this procedure was eye pain and discomfort which occurred in 78% of cases; this pain was mild in

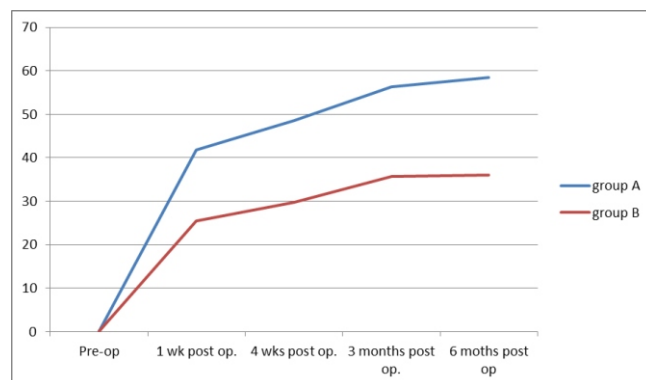
95% of patients with pain. All cases showed complete regression of rubeosis iridis within 3 months after SCB but at 6 months 5% of eyes showed recurrence of rubeosis iridis probably due to continuous retinal ischemia.

Discussion

NVG is one of the common causes of refractory glaucoma whereas satisfactory IOP level is not usually been achieved by conventional maximum ocular antihypertensive medications, PRP, glaucoma drainage surgeries, and cyclodestructive procedures. (8) Bevacizumab (Avastin) was widely used to treat anterior segment neovascularization with or without glaucoma which was reported to achieve rapid improvement in rubeosis iridis. (9) IVA was used as adjunctive to trabeculectomy or AVG surgery to control NVG; Hatem and Amin reported that Intravitreal bevacizumab has a role in regression of iris neovessels and IOP control in NVG and it had an important role in increasing the success rate of subcleral trabeculectomy with mitomycin C while Zhang et al. reported that preoperative IVA combined with AGV implantation was a good treatment modality in the management of eyes with NVG and it increase the success of surgery. (10,11) in addition, Bevacizumab was also administered subconjunctivally as adjunctive to trabeculectomy and many studies reported that it was also effective. (12)

In this study a different approach was tried; Subconjunctival 1.25 mg of Bevacizumab (SCB) was administered at the end of AVG surgery and the results were compared to those patients who underwent AVG surgery for NVG without the use of Bevacizumab. In this study it was obvious that the use of SCB was significantly associated with lower IOP level at 1 week, 4 weeks, 3 months and 6 months when compared with IOP of the eyes that did not receive SCB (P value < 0.05), (fig.1). This effect is thought to be attributed to the resolution of rubeosis iridis by anti-vascular endothelial growth factor (VEGF) effect of Bevacizumab since rubeosis iridis plays an important role in developing NVG.

Fig 1, The level of IOP pre and post-operatively in group A and B.



In addition, the use of SCB was significantly reduced the demand for ocular antihypertensive medications at 1 week, 4 weeks, 3 months and 6 months post-operatively when compared with

patients who did not receive SCB (P value < 0.05), (fig.2). This effect is related to the better control of post-operative IOP. Also well-functioning tube was observed after a AVG surgery when combined with SCB.

Fig 2, The number of medications needed to control the IOP pre and post-operatively in group A and B

In this study we used the criteria used by Huang MC et al in 1999 to evaluate the success of the procedure in which they considered the procedure to be successful where the IOP was between 5-21 mmHg with or without medication, no further glaucoma surgery is needed, no devastating complications occurred, and no loss of light perception. (13) Although Ahmed valve operations for NVG have a low success rate due to excessive intra- and postoperative inflammation and bleeding from NVI, it was clearly noticed that the success rate was significantly better in patients who received SCB. (14,15).

SCB is thought to be more safe than IVA since IVA is associated with additional risk for endophthalmitis and higher chance for more elevation in IOP which may adversely affect vision.

SCB was very effective and safe when used as adjunct to AVG surgery in patients with NVG and it improved the function of the AVG tube. More studies are needed to compare the effect of IVA with SCB in the management of NVG.

CONCLUSION

Subconjunctival Bevacizumab has an excellent additive effect in regression of rubeosis iridis and achievement of better IOP control when administered at the time of Ahmed glaucoma valve surgery in patients with neovascular glaucoma and it significantly increases the success rate of the surgery.

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