

Combined Trabeculectomy with beta irradiation with and without intravitreal bevacizumab for neovascular glaucoma

Sawsan Abdel Sabour¹, Mohamed Yasser S. Saif^{2*}, Ahmed Tamer Saif³, Passant S Saif⁴

¹ Azhar University

² Beni Suef University

³ Fayoum University

⁴ Misr University for Science and Technology

7

8

9

10

11

ABSTRACT

Purpose: To evaluate the efficacy and safety of intravitreal bevacizumab (IVB) and adjunctive Strontium-90 (Sr^{90}) beta radiotherapy with trabeculectomy in the management of neovascular glaucoma (NVG).

Methods: Thirty seven eyes with NVG were randomly selected and divided into two groups according to the treatment given

Group 1: Trabeculectomy with Beta-irradiation (n = 18 eyes).

Group 2: Preoperative (IVB) followed after two weeks by trabeculectomy and Beta-irradiation (n = 19 eyes).

Intraocular pressure (IOP), and regression of rubiosis iridis (NVI) are the used outcome measures.

Results: By 6 months postoperatively, the mean IOP levels decreased from 38.6 mmHg pre-operatively to 11.3 mmHg on the first postoperative week and 16.2 at the end of follow up for all cases. No significant difference between both groups as regard of success, while group 2 (IVB) showed more regression of NVI and less incidence of complications.

Conclusion: Preoperative IVB combined with filtration surgery and adjuvant Strontium-90 (Sr^{90}) beta radiotherapy is a safe and effective method of controlling intraocular pressure in NVG.

Keywords: intravitreal bevacizumab (IVB) , Strontium-90 (Sr^{90}) beta radiotherapy , rubiosis iridis , neovascular glaucoma

1. INTRODUCTION

Neovascular glaucoma (NVG) is a severe form of secondary glaucoma characterized by proliferation of fibrovascular tissue in the anterior chamber angle⁽¹⁾. Preventing neovascularization is the most successful treatment for NVG. In light of the association of vascular endothelial growth factor (VEGF) with retinal ischemia, the advent of anti-VEGF drugs may provide a welcome addition in the treatment strategy for this potentially devastating condition^(2,3).

Beta radiation has been shown *in vitro* and *in vivo* to inhibit proliferation of human Tenon's fibroblasts, which enter a period of growth arrest but do not die. Beta radiation may be

* Tel.: +201006699288.

E-mail address: ysaif@med.bsu.edu.eg

particularly appropriate for use to improve the results of trabeculectomy while potentially avoiding some of the side effects of other antimetabolites ⁽⁴⁾.
Purpose: To evaluate the efficacy and safety of IVB and adjunctive Strontium-90 (Sr^{90}) beta radiotherapy with trabeculectomy in the management of NVG.

2. MATERIAL AND METHODS / EXPERIMENTAL DETAILS / METHODOLOGY (ARIAL, BOLD, 11 FONT, LEFT ALIGNED, CAPS)

Patient with NVG and rubiosis iridis were included in this study. Patients with previous glaucoma surgery or previous ocular trauma were excluded from the study
Patients were selected from the outpatient clinics of Beni suef university hospital, Azhar University Hospital, Fayoum university hospital, and Misr university hospital

The Ethic committee in the 4 universities approved the study and informant consents was taken from patients before IVB injection and before surgery

A full ophthalmic examination was done to all patients including visual acuity, IOP , anterior segment and fundus examination, ultrasonography for some patients with opaque media

Thirty seven patients (37 eyes) with NVG were randomly selected and divided into two groups according to treatment:

Group 1: Trabeculectomy with Beta-irradiation (n = 18 eyes).

Group 2: Preoperative IVB (1.25 mg) followed after two weeks by trabeculectomy and Beta-irradiation (n = 19 eyes).

The ethical

Preoperative IVB (1.25 mg in 0.05ml) (figure 1 a) was delivered using a sharp 27-gauge needle through the inferotemporal quadrant 4 mm from the limbus for group 2 (figure 1c).

Trabeculectomy was planned 2 weeks after IVB.

Beta irradiation applicator (figure 1 a) was applied under the conjunctiva and over the sclera before fashioning of the scleral flap in 1000 rad dose (figure 1b). Booster dose can be applied over the bleb if indicated.

Cases were followed at first post-operative day, after one week, one month, 3, and 6 months at least. Examination of cases included intraoperative and postoperative complications, intraocular pressure (IOP), regression or recurrence of iris neovascularization (NVI), additional topical medications required after trabeculectomy.

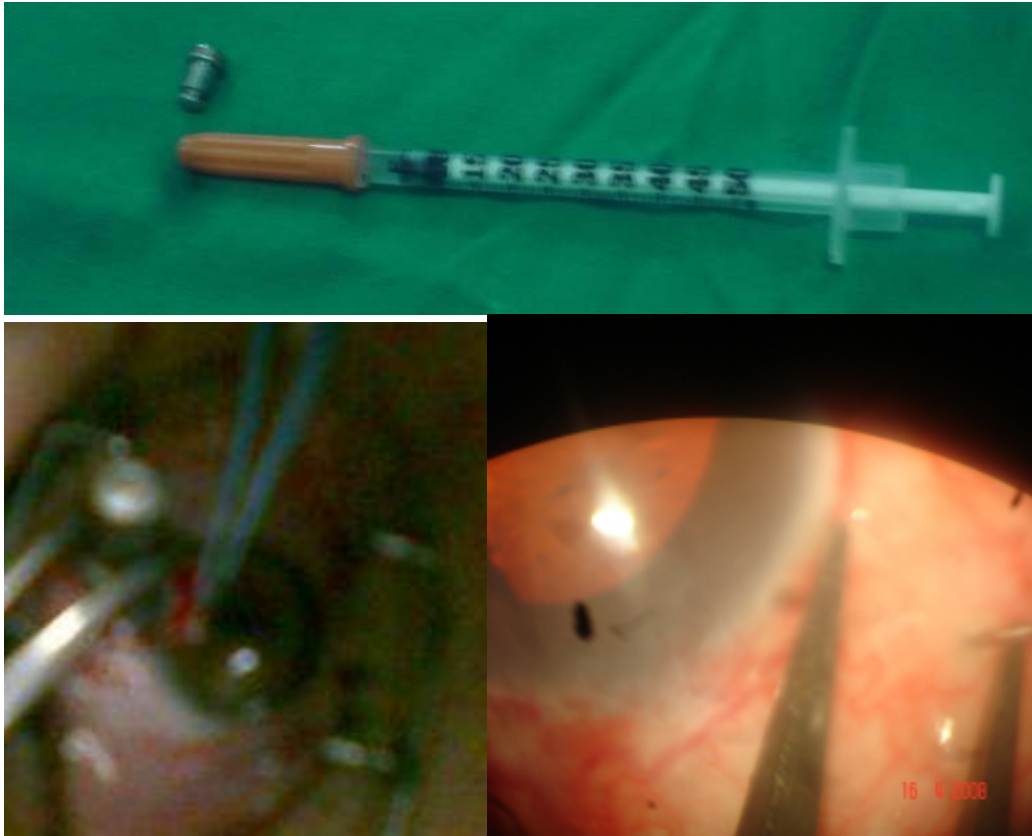


Figure (1): (1a: Top picture) Beta Irradiation and Avastin used in the study (1b: bottom left) Application of Beta Irradiation, (1c:bottom right) IVB injection 4 mm from the limbus.

Patient data was collected in excel sheet and statistical analysis was done using the Microsoft excel 2010 and the SPSS v17 program

3. RESULTS AND DISCUSSION

Thirty seven patients randomly included in this study with a Mean age of the patients was 61.4 ± 8.3 years (range 48–78 years) as shown in table 1. Mean follow-up was 18 months (6–36 months)

Table (1): shows the demographic data for patients included in the study

	Group 1 (Trab + Beta Irrad. N=19)		Group 2 (Trab + Beta Irrad + IVBs.n=18)		All
	females	males	females	males	
count	9	10	10	8	37
Mean age	62.6	60.0	58.8	61.3	61.4

median	65	60	56.5	59	62
Standard Deviation	9.8	9.1	9.0	8.7	8.3
Max age	73	70	75	78	78
Min age	50	50	48	52	48

Mean intraocular pressure (IOP) decreased from 38.6 mmHg pre-operatively to 11.3 mmHg on the first postoperative week and 16.2 at the end of follow up (figure 2).

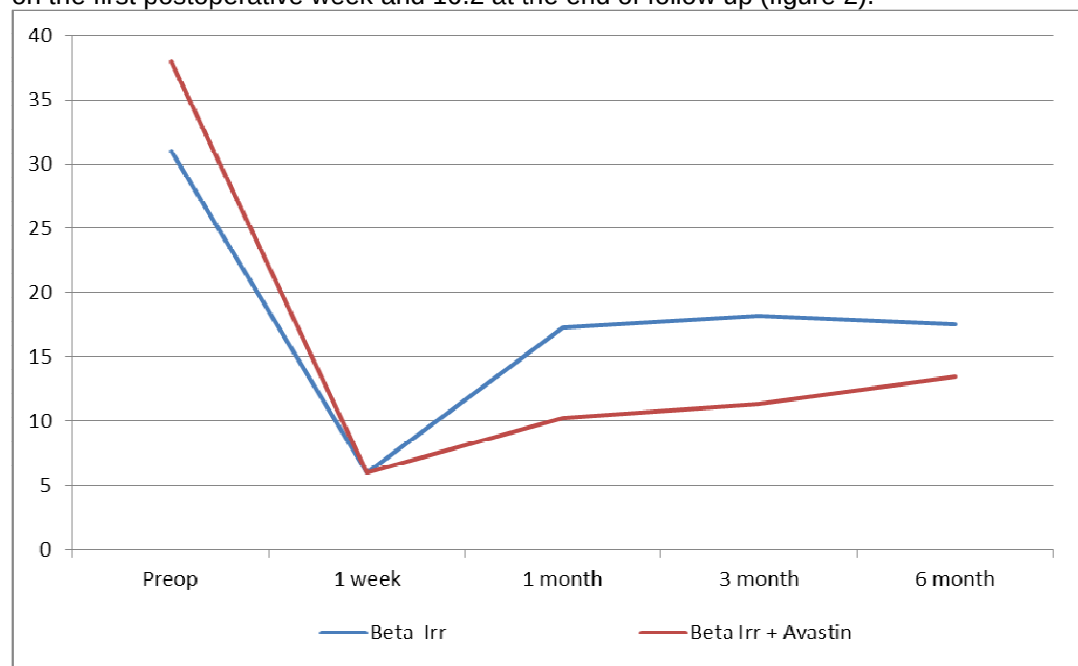


Figure (2): Mean intraocular pressure (IOP) in mmHg changes for the 2 groups. (Preop= Preoperative or baseline)

Twenty patients had controlled IOP without anti-glaucoma medication, fifteen cases were controlled with anti-glaucoma medication, and 3 cases need surgery (table 2) . Success was defined as controlled iop to normal level with or without medication and regression of rubiosis iridis . Success rates at 6 months were 94.44% (17 out of 18) in the IVB group versus 89.47% (17 out of 19) in the other group. Change in IOP, additional glaucoma surgeries required, and IOP-lowering topical medications required after trabeculectomy did not differ significantly between the 2 groups ($P > 0.05$).

During the follow up (6– 36 months), postoperative hyphema on day 1 or with a duration of > 1 week occurred in four patients but it is significantly less in the IVB patients (one out of four).

Shallow AC was recorded in 20 cases and is regained within one week, while it is lost in 2 cases.

The incidence of serious complications such as endophthalmitis, phthisis bulbi and a marked decrease in visual acuity did not increase in the IVB group. Early and late postoperative complications were recorded in table 2 .

105 Absolute regression of NVI (figure 3a) was observed within 1 week after IVB in 13 patients
 106 versus 5 in non IVB group and reduced NVI but still persisted in five patients in IVB versus
 107 14 in the other group. Recurrent NVI was subsequently detected in patients who had
 108 uncontrolled IOP. However, the IVB group had significantly higher frequency and rapidity of
 109 iris neovascular regression.

110
 111

Table (2): . Early and late postoperative complications

Complications		No	Percentage
Early	• shallow AC	20	54.05%
	• hyphema	4	10.81%
	• Low IOP	8	21.62%
	• Choroidal detachment	3	8.11%
	• lost AC	2	5.41%
Late	• cystic bleb	3	8.11%
	• Cataract	6	16.22%
	• no complications	17	45.95%
	• endophthalmitis	0	0.00%
	• need medical ttt	11	29.74%
	• need re-surgery	3	8.11%

112

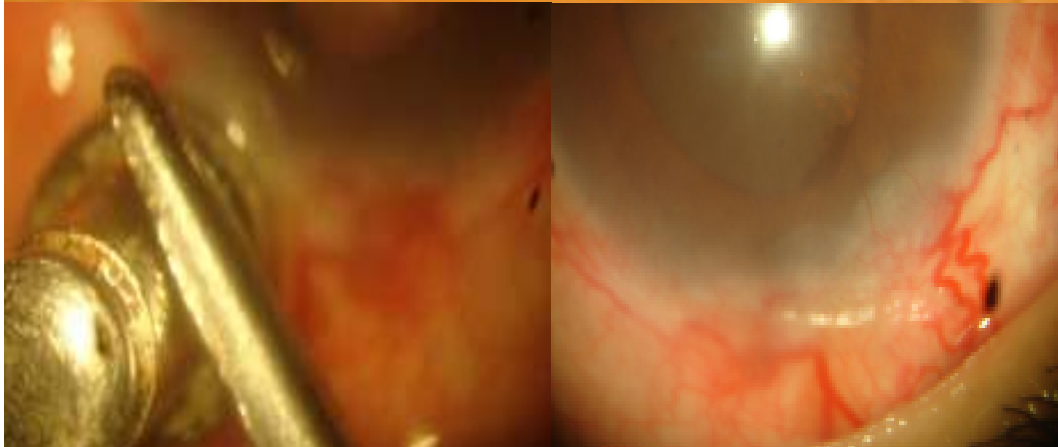


Figure (3a: upper): Absolute regression of NVI, (3b: bottom): Postoperative booster dose Beta irradiation

Discussion

Strontium-90 (Sr^{90}) beta radiotherapy is a noninvasive treatment using a hand held applicator. It has been used widely for the treatment of pterygium and for controlling wound healing after glaucoma drainage surgery. In this latter role, beta radiation may be particularly appropriate for use in developing countries (not expensive) to improve the results of trabeculectomy while potentially avoiding some of the side effects of other antimetabolites⁽⁴⁾ No significant variation in success rates of IOP control at 6 months postoperatively. It was 94.44% with IVB (group 2) versus 89.47% without IVB (group 1). This coincides with

127 [Fakhraie G et al 2010⁵](#) and [Chen CH et al 2010⁶](#), about preoperative IVB role in INV
128 regression and may be used adjunctively to improve resolution but failed to lower the IOP.
129 IVB is well tolerated, effectively stabilized INV activity, and cannot control IOP but may be
130 used adjunctively to improve subsequent surgical results ⁽⁷⁾.
131 Postoperative hyphema occurred in four cases only one with preoperative IVB, and the rest
132 3 without use of IVB. We agree with Siato and associates ⁽⁸⁾, as regard the incidence of
133 serious complications such as endophthalmitis, phthisis bulbi those did not increase in the
134 IVB group .
135 The treatment of the causative ischemic stimulus is necessary in every stage of disease.
136 One further indication for bevacizumab is the postoperative inhibition of angiogenesis after
137 glaucoma surgery. Possible routes of administration are subconjunctival application during
138 trabeculectomy, postoperative needling, or intravitreal injection during a filtering operation⁽⁹⁾.
139

140
141

142 **4. CONCLUSION**

143
144 Preoperative IVB combined with filtration surgery and adjuvant Strontium-90 (Sr⁹⁰) beta
145 radiotherapy might be a safe and effective method of controlling intraocular pressure in
146 NVG.

147
148

149 **COMPETING INTERESTS**

150
151 **THE AUTHORS DECLARE THAT THERE IS NO CONFLICT OF INTERESTS**
152 **REGARDING THE PUBLICATION OF THIS ARTICLE.**
153

154
155

156 **AUTHORS' CONTRIBUTIONS**

157 All authors manage and examine the cases, follow up the cases, share in writing and editing.
158 of the manuscript."

159
160

161 **CONSENT (WHERE EVER APPLICABLE)**

162 "All authors declare that 'written informed consent was obtained from all patients before the
163 injection or before the surgery done. A copy of the written consent is available for review by
164 the Editorial office/Chief Editor/Editorial Board members of this journal."

165
166

167 **ETHICAL APPROVAL (WHERE EVER APPLICABLE)**

168 The ethic committee approval and the ophthalmology department approvals is available
169 when needed
170

171
172

173 **REFERENCES**

174 **1 - Wand M., Neovascular glaucoma. In:** Ritch R, Shields MB, Krupin T, eds. The
Glaucomas – Clinical Science. 2nd. Ed. St. Louis: Mosby; 1996: 1073-1129. Ch 51.

175 **2 - Sivak-Callcott JA, O'Day DM, Gass JD, et al.** Evidence-based recommendations for
 176 the diagnosis and treatment of neovascular glaucoma. *Ophthalmology*. 2001; 108:1767-
 177 1776.

178 **3 - Hayreh SS.** Neovascular glaucoma. *Prog Retin Eye Res*. 2007; 26(5): 470-485.

179 **4 - Kirwan J F , Constable P H , Murdoch I E and Khaw P T** Beta irradiation: new uses for
 180 an old treatment: a review; *Eye* (2003) 17, 207–215. doi:10.1038/sj.eye.6700306
 181 <http://www.nature.com/eye/journal/v17/n2/abs/6700306a.html>

182 **5 - Fakhraie G, Katz LJ, Prasad A, Eslami Y, Sabour S, Zarei R, Moghimi S.** Surgical
 183 outcomes of intravitreal bevacizumab and guarded filtration surgery in neovascular
 184 glaucoma. *J Glaucoma*. 2010 Mar;19(3):212-8. doi: 10.1097/IJG.0b013e3181aae928.

185 **6 - Chen CH, Lai IC, Wu PC, Chen YJ, Chen YH, Lee JJ, Liu YC, Kuo HK.** Adjunctive
 186 intravitreal bevacizumab-combined trabeculectomy versus trabeculectomy alone in the
 187 treatment of neovascular glaucoma. *J Ocul Pharmacol Ther*. 2010 Feb;26(1):111-8. doi:
 188 10.1089/jop.2009.0055.

189 **7 - Wakabayashi T, Oshima Y, Sakaguchi H, Ikuno Y, Miki A, Gomi F, Otori Y, Kamei**
 190 **M, Kusaka S, Tano Y.** Intravitreal bevacizumab to treat iris neovascularization and
 191 neovascular glaucoma secondary to ischemic retinal diseases in 41 consecutive cases.
 192 *Ophthalmology*. 2008 Sep;115(9):1571-80, 1580.e1-3. doi: 10.1016/j.opthta.2008.02.026.
 193 Epub 2008 Apr 28

194 **8 - Saito Y, Higashide T, Takeda H, Ohkubo S, Sugiyama K.** Beneficial effects of
 195 preoperative intravitreal bevacizumab on trabeculectomy outcomes in neovascular
 196 glaucoma. *Acta Ophthalmol*. 2010 Feb;88(1):96-102. doi: 10.1111/j.1755-
 197 3768.2009.01648.x. Epub 2009 Sep 23.

198 **9 - Lüke J, Lüke M, Grisanti S.** Antiangiogenic treatment for neovascular glaucoma and after
 199 filtering surgery; *Ophthalmologe*. 2009 May;106(5):407-12. doi: 10.1007/s00347-009-1940-2.
 200