The Value of Intracameral Injection of Bevacizumab for Treatment of Rubeosis Iridis in Neovascular Glaucoma in Nassiryah City

Wajida Saad Bunyan*

Wajida Saad Bunyan
College of Medicine, University of Thi-Qar, Iraq.
E-mail: Wajieda_s@hotmail.com

Correspondence:
Wajida Saad Bunyan
College of Medicine, University of Thi-Qar, Iraq.
E-mail: Wajieda_s@hotmail.com

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ABSTRACT

Purpose: This work targets assessing the estimation of intracameral bevacizumab infusion in treatment of rubeosis iridis in neovascular glaucoma.

Patients and strategies: A planned report was done on 30 eyes of 30 patients with rubeosis iridis. Intracameral infusion of bevacizumab was infused for all patients. Iris flourescein angiography and specular microscopy were performed to all patients preoperatively and postoperatively. Patients were followed up at five days, one month, a quarter of a year, and a half year spans following the system.

Results: Iris fluorescein angiography demonstrated neovascularization relapse just in the early development. Notwithstanding, specular microscopy indicated practically stable endothelial trustworthiness aside from a couple of cases.

Conclusion: The utilization of intracameral bevacizumab for rubeosis iridis still needs more preliminaries to build up long haul security and viability in retinal ischemia and neovascular glaucoma.

Keywords: Bevacizumab, neovascularization, Neovascular glaucoma, Iris fluorescein angiography, Specular microscopy.

INTRODUCTION

Neovascular glaucoma (NVG) is an auxiliary glaucoma by and large connected with poor visual anticipation. The advancement of new vessels over the iris and the iridocorneal edge can block fluid humor outpouring and lead to expanded intraocular pressure. It is related with the improvement of a fibrovascular film on the front surface of the iris and iridocorneal point of foremost chamber.(Hayreh ,2007)Attack of the front chamber by a fibrovascular layer at first hinders fluid surge in an open-edge style and later agreements to create auxiliary synechial edge conclusion glaucoma with high IOP. (Shazly and Latina ,2009). The basic pathogenesis much of the time is back section ischemia, which is most usually optional to proliferative diabetic retinopathy or focal vein retinal occlusion (Albert and Jakobiec ,1999). Neovascularization is a multi-step measure that includes complex collaborations of an assortment of angiogenic entertainers. New vessel arrangement in the eye is influenced to an enormous degree by an unbalance between favorable to angiogenic factors, (for example, vascular endothelial development factor-VEGF) and other enemy of angiogenic factors, (for example, shade epithelium inferred factor).(Bakri et al.,2007)Watery degrees of VEGF are profoundly raised and altogether related with the degree of neovascularization and IOP in NVG patients (Sasamoto et al.,2012). Convergence of VEGF can decrease after the relapse of iris neo-vessel. (Chen et al.,2007). Bevacizumab (Avastin) is a monoclonal VEGF inhibitor that was first utilized in ophthalmology to treat subretinal neovascularization in eyes with age-related macular diseases (Ehlers et al.,2008). Bevacizumab, a VEGF-An inhibitor, causes relapse of iris neovasculrization when infused into the glassy or the foremost chamber. Nonetheless, the span of activity of bevacizumab is fleeting, enduring around 4 weeks. (Ehlers et al.,2008). The pharmacokinetics of bevacizumab has not been inspected in direct connection to the term of movement against iris neovasculrization (Bakri et al.,2007; Krohne et al.,2008).

Aim of study

1. Asses the estimation of intracameral bevacizumab to diminish the measure of front section neovascularization obvious on Iris Fluorescein Angiography (IFA.(
2. Monitor the impact with IFA.
3. Evaluate the corneal endothelium by specular microscopy when infusion.

PATIENTS AND METHODS

Thirty eyes of 30 continuous patients with rubeosis iridis auxiliary to NVG either because of diabetic retinopathy or focal retinal vein impediment, alluded to Ophthalmology Division in Al Habobi Showing clinic, Nassiryah city were enrolled in this planned investigation. All patients were found in the period from September 2018 to September 2019.

Patients' age ran from 45 to 70 years with a mean of 57.5 years. Eighteen of the patients were guys and the staying twelve were females. Of the 30 NVG cases remembered for this investigation, 15 were optional to diabetic retinopathy, 12 were because of focal retinal vein impediment, 1 was expected concoction injury, and the staying 2 was following longstanding retinal separation medical procedure. The best revised visual keenness was running from 6/12 to

observation light. The subsequent period extending from 5 days to a half year.

Ocular examination

All patients in this examination gone through the accompanying introductory clinical evaluation:

- Landolt's outline for visual keenness test
- Anterior section assessment
- Intraocular pressure estimation with applanation tonometer
- Fundus assessment by roundabout ophthalmoscope and 20D focal point after instillation of 1% tropicamide drops for prompt mydriasis.
- Iris fluorescein angiography (sodium fluorescein 5ml, 10%)
- Specular microscopy

Treatment

The strategy was done in a careful ward after instillation of effective sedative drops, purification, sterile hanging and cover speculum application. Limbal paracentesis was performed by an insulin needle, at that point infusion of 1mg (0.04ml) of Avastin into the foremost chamber, trailed by remedy of oral acetazolamide 500mg tablet following the method. Postoperative treatment included anti-infection/steroid eye drops three times each day for multi week. Therapy was booked somewhere in the range of 2 and 5 days after starting iris flourescein angiography and specular microscopy.

Evaluation

The objective of the system was to instigate relapse of the iris neovascularization, subsequently decrease the intraocular pressure. Follow up was orchestrated at 5 days, and a half year span following the intracameral infusion. At each visit intraocular pressure was estimated with applanation tonometer.

The subsequent visit included performing iris flourescein angiography and specular microscopy to the worked eye. A few patients required ophthalmic ultrasound to assess the fundus because of visual obscuration by different media opacities as waterfall or glassy drain. Others required ultrasound biomicroscopy (UBM) or foremost OCT to identify edge or iris irregularities.

Iris fluorescein angiography (IFA)

The fundus camera utilized in this investigation was ZEISS 500. The photographs were taken utilizing an advanced camera back Sony Force had associated with exceptional PC and prepared under unique programming.

Specular magnifying lens

Specular magnifying lens (NIDEK CEM-530 paracentral). It was utilized to record the focal and paracentral corneal endothelial picture and measure the corneal thickness.

RESULTS

Thirty eyes of 30 patients were treated in this examination. Patients' ages extended from 45 to 70 years with a mean of 57.50 years. Eighteen of these patients were guys (60%) and the staying twelve (40%) were females as appeared in Fig.1

The best adjusted visual sharpness was going from 6/12 to observation light. The subsequent period traversed from 5 days to 6 months.

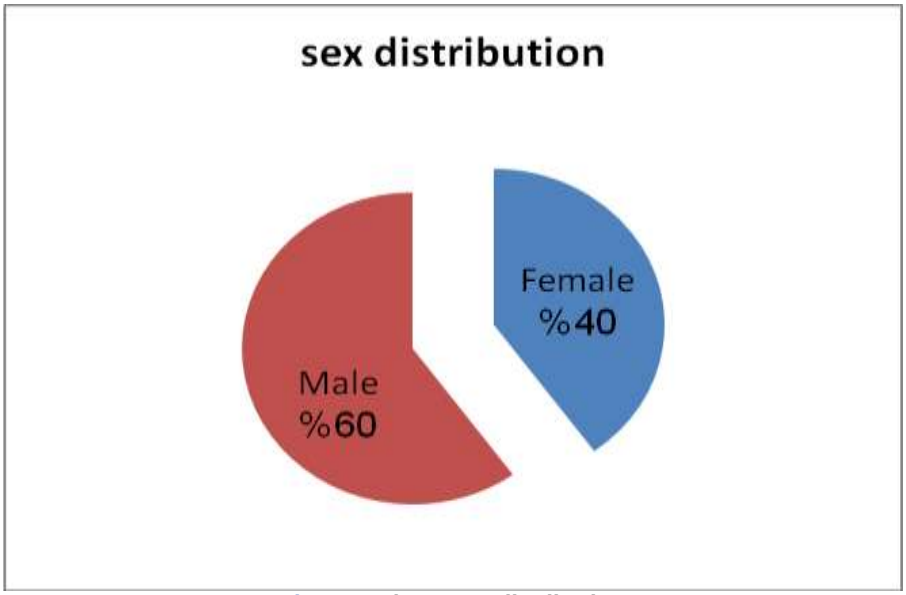

Figure 1: Shows Sex distribution

The reasons for this condition was variable. 15 patients who created rubeosis was expected to PDR, 12 patients due to CRVO, and 1 was because of synthetic injury, and 2 was because of long standing retinal separation medical procedure as appeared in Fig.2

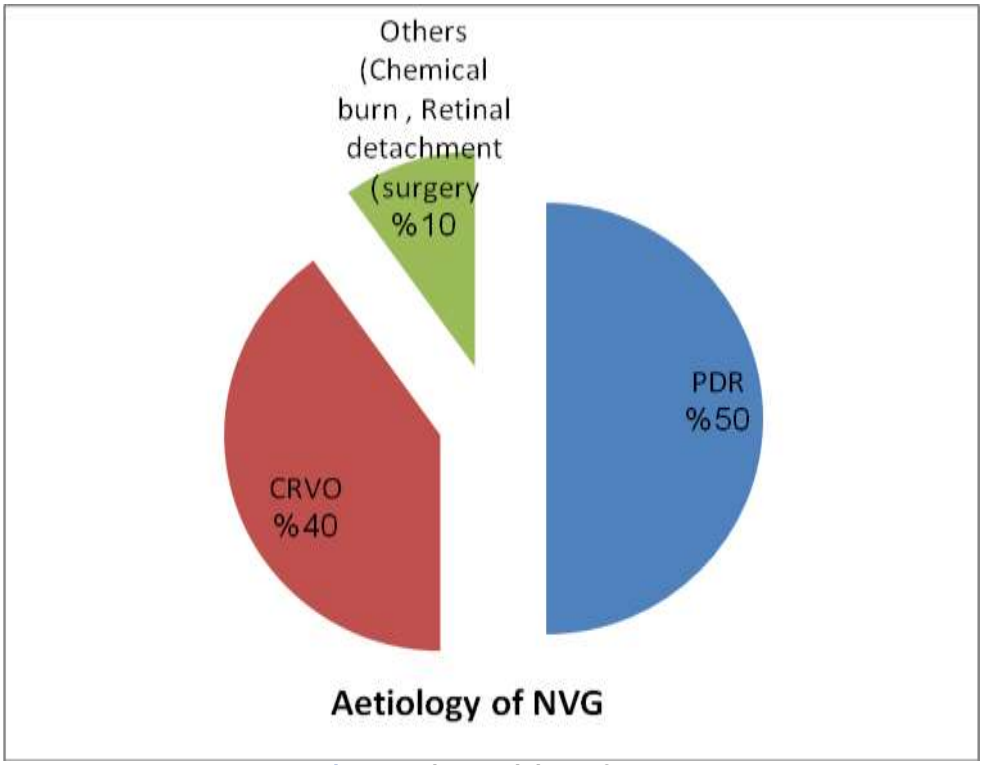

Figure 2: Shows Etiology of NVG

Table 1: Shows patients Data

Case N0.	patients		IOP (in mm Hg)		Corneal endothelial integrity		Rubeosis iridis by Fluorescein angiography	
	Age	sex	Pre-ICB	Post-ICB	Early : 5 ds-1m	Late: 3m-6m	Early : 5 ds-1m	Late: 3m-6m
1	45	F	23	22	Intact	Intact	regression	return
2	50	M	23	22	Affect	Affect	regression	return
3	55	F	24	20	Intact	Affect	regression	return
4	56	F	25	20	Intact	Intact	regression	return
5	64	M	20	18	Intact	Intact	regression	return
6	50	M	20	23	Intact	Intact	regression	return
7	60	F	23	23	Intact	Intact	regression	return
8	70	M	27	22	Intact	Intact	regression	return
9	65	M	24	23	Intact	Intact	regression	return
10	69	M	23	20	Intact	Intact	regression	return
11	60	M	23	23	Intact	Intact	regression	return
12	55	M	20	20	Intact	Intact	regression	return
13	45	M	24	26	Intact	Intact	regression	return
14	46	F	24	25	Intact	Intact	regression	return
15	48	M	25	24	Intact	Intact	regression	return
16	50	M	21	22	Intact	Intact	No regression	No regression
17	55	M	25	26	Intact	Intact	No regression	No regression
18	53	F	24	23	Intact	Intact	regression	return
19	57	M	20	21	Intact	Intact	regression	return
20	58	F	24	26	Intact	Intact	regression	return
21	60	F	21	22	Affect	Affect	regression	return
22	63	M	25	26	Intact	Intact	regression	return
23	53	M	25	24	Intact	Intact	regression	return
24	55	M	20	20	Intact	Affect	regression	return
25	56	F	22	21	Intact	Intact	regression	return
26	63	M	25	24	Intact	Intact	regression	return
27	62	F	21	22	Intact	Intact	regression	return
28	60	M	20	21	Intact	Intact	regression	return

29	50	M	24	23	Intact	Intact	No regression	No regression
30	51	F	21	22	Affect	Affect	No regression	No regression

Statistical Analysis

1. Patients' outcome

a. The outcome of the 30 patients was measured by analyzing two main criteria, before and after the intracameral injection. These criteria were: regression of neo-vascularization by using IFA, and endothelial cell count by specular microscopy. Correlated to these criteria was monitoring two main data: IOP and best corrected visual acuity.

The first criterion evaluated in our study was the regression of neovascularization. It showed marked regression during the fifth day of follow up. Then the regression effect started to deteriorate over the next one month follow up and showed almost complete return of neovascularization in the last two follow up periods; 3 and 6 months as shown in Fig.3

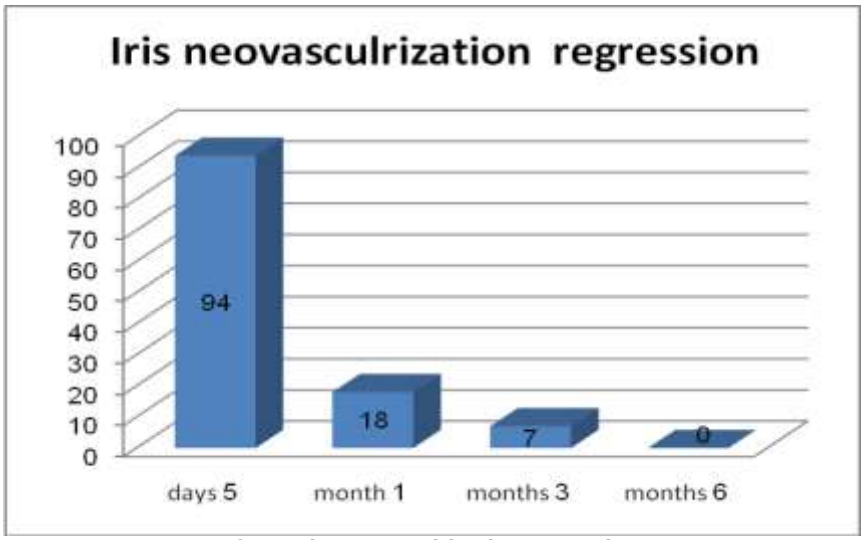

Fig. 3: Iris neovasculrization regression

b. The subsequent standard assessed in our investigation was endothelial cell check. It demonstrated no checked drop in tally during the entire follow up periods as appeared in Fig.4

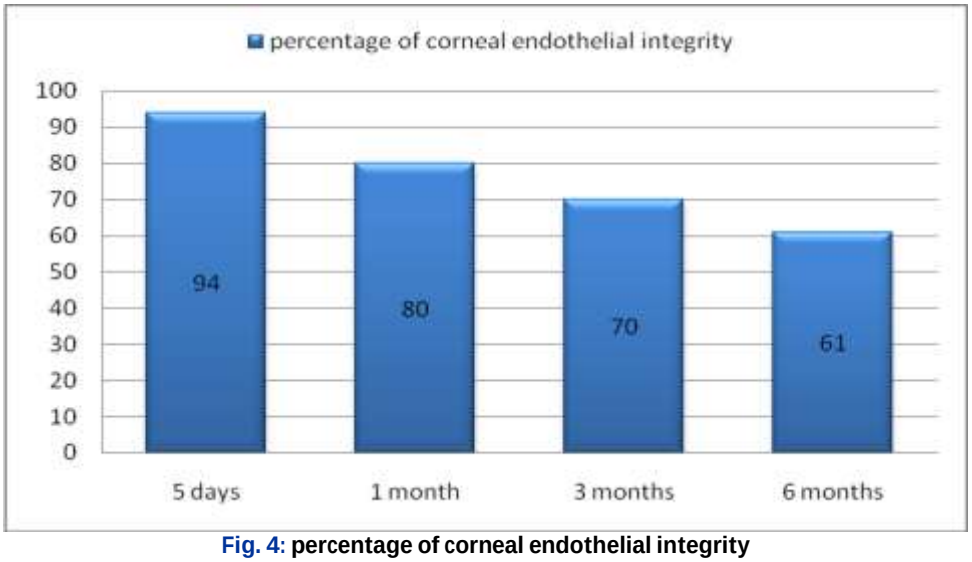

Fig. 4: percentage of corneal endothelial integrity

c. As to first relationship, the IOP, it was reliably lower after infusion during the entire follow up period (P=0.05) as appeared in Fig.5

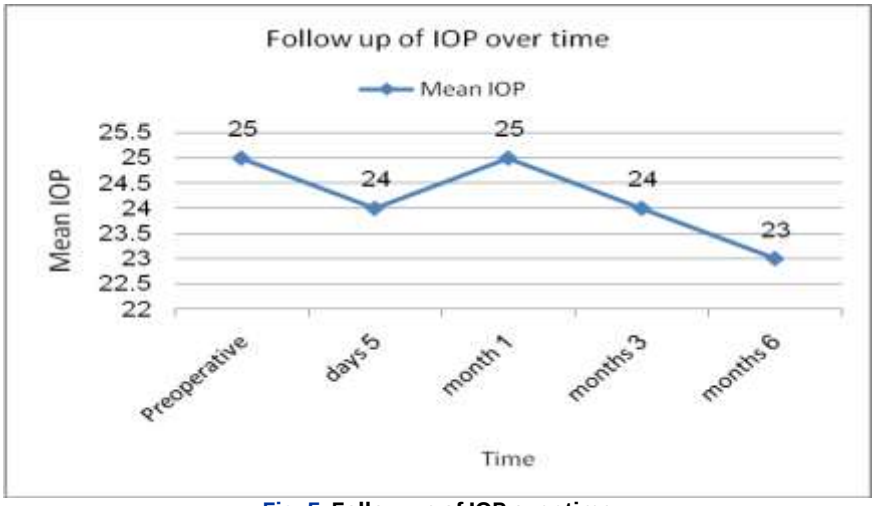

Fig. 5: Follow up of IOP over time

d. The other connection was the best revised visual sharpness (BCVA) which was surveyed via Landolt's diagram at that point changed over to logMAR. It demonstrated a decline in BCVA after some time, which was not measurably noteworthy (P=0.13)

Table 2: BCVA over time

BCVA	Mean	Std. deviation	N
Preoperative	1.75	0.56	24
5 days	1.75	0.56	24
1 month	1.85	0.58	24
3 months	1.93	0.67	24
6 months	1.98	0.70	24

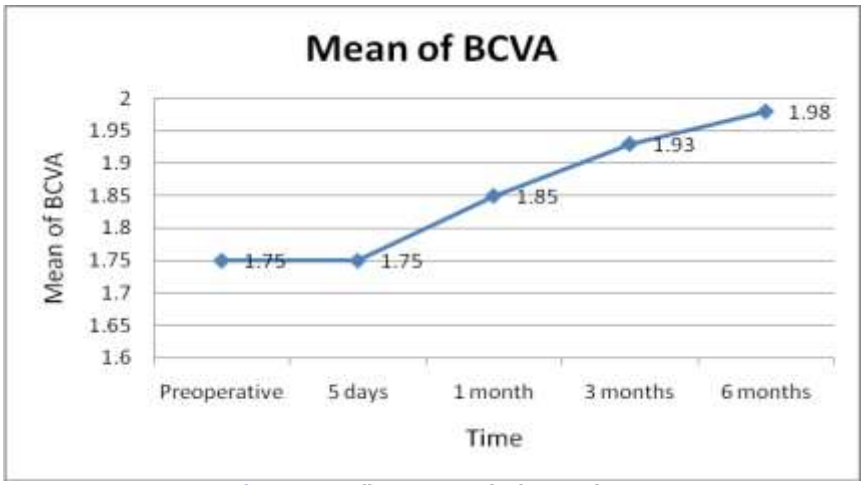

Fig.6: BCVA (log MAR units) over time

2. Correlative Data

a. A relationship between's neovascular relapse and IOP was broke down, checked by IFA and applanation tonometer individually. This was factually appropriate just for the initial two follow up periods: 5 days and one month individually. It indicated decrease in IOP in patients who had neovascular relapse.

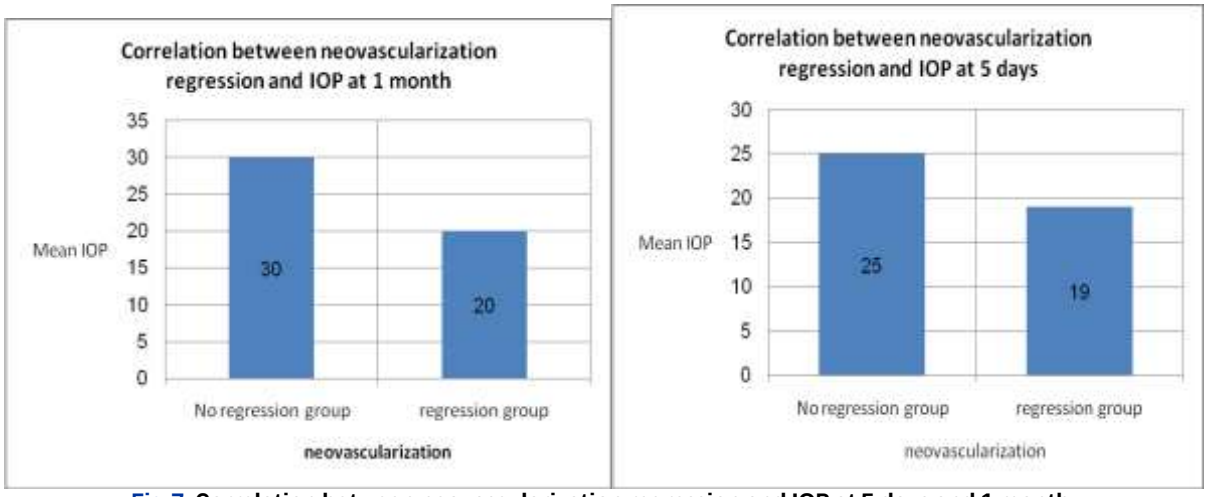

Fig.7: Correlation between neovascularization regression and IOP at 5 days and 1 month.

b. A connection among's IOP and endothelial cell tally was likewise factually dissected, checked by applannation tonometer and specular microscopy separately. This was just pertinent in the multi month follow up period, indicating two gatherings: a gathering with low endothelial cell check with high IOP, and another gathering with no impact on endothelial cell tally with typical IOP.

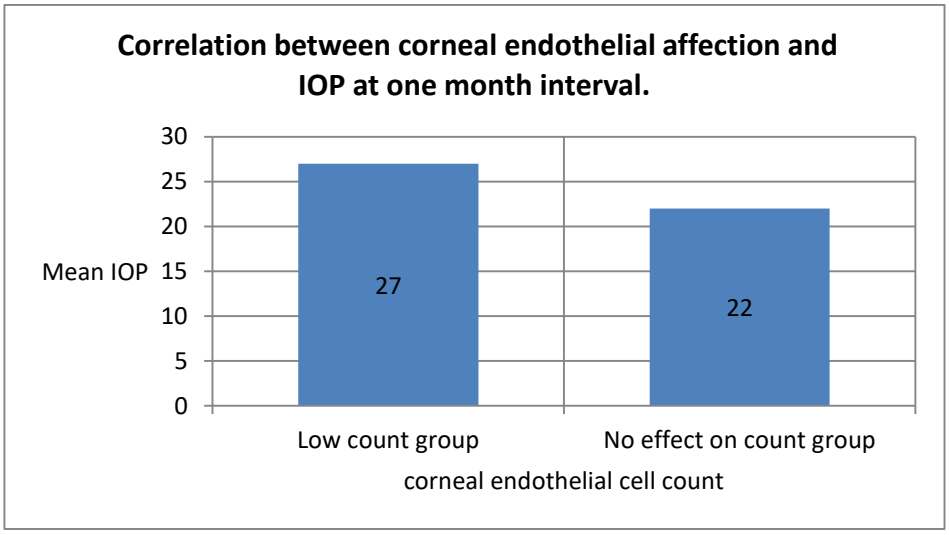

Fig.8: Correlation between corneal endothelial affection and IOP at one month interval.

c. In preliminary to relate between neovascular relapse and endothelial cell tally; checked by IFA and specular microscopy, no relationship was seen during any of the subsequent periods.

Complication

All patients (30) created repetitive iris neovascurization. Two patients created persevering increment IOP. Three patients (10%) created hyphema

DISCUSSION

NVG is an overwhelming illness that is frequently profoundly impervious to treatment, bringing about serious visual loss (Ehlers et al.,2008) The improvement of new vessels over the iris and the iridocorneal point can impede fluid humor outpouring and lead to expanded intraocular pressure. The basic pathogenesis by and large is back section ischemia, which is most generally auxiliary to proliferative diabetic retinopathy or focal vein retinal occlusion (Albert and Jakobiec ,1999).

Neovascularization is a multi-step measure that includes complex communications of an assortment of angiogenic entertainers. New vessel arrangement in the eye is influenced to a huge degree by an unbalance between favorable to angiogenic factors, (for example, vascular endothelial development factor-VEGF) and other enemy of angiogenic factors, (for example, shade epithelium-inferred factor) (Bakri et al.,2007).

Clinical treatment of the raised IOP experienced in NVG is stalling, especially if the points are shut by synechiae. By the by, controlling the IOP until more complete treatment can produce results is significant for shielding the optic nerve from harm, diminishing related agony, and conceivably improving vision auxiliary to IOP-subordinate corneal edema. Careful mediation is demonstrated when clinical

treatment is lacking to control IOP, especially if synechial point conclusion from NVA has happened. Trabeculectomy and other separating medical procedures are decently effective in the long haul in patients with NVG (Lisa et al.,2011).

The point of this examination to assess the viability of intracameral infusion bevacizumab for the board of rubeosis iridis in NVG.

The aftereffects of this investigation indicated that bevacizumab was considerably more viable in the early development (5 days and multi month) in causing relapse of new vessels. Notwithstanding, its impact nearly decayed in the late development (3 months and a half year), in which there was return of the iris neovascularization.

In this examination IFA was utilized as a subsequent instrument to survey relapse of new vessels after intracameral infusion of bevacizumab. It was discovered that a solitary use of the medication caused an emotional decrease of spillage from rubeotic vessels. Notwithstanding, this impact was not durable and return of new vessels happened 3 months after the fact in the majority of the cases.

Another subsequent apparatus utilized in this investigation was specular microscopy to evaluate the impact of intracameral infusion of bevacizumab on corneal endothelium. There was insignificant changes on the endothelial cell include in most of cases.

Connecting the past two measures, the neovascular relapse and the endothelial cell check, to the IOP, it was discovered that there is no solid relationship with it during the subsequent period.

As to BCVA, the greater part of the patients remembered for this examination there were poor visual sharpness. There were no improvement in BVCA. Despite what might be expected, it was either steady or crumbled during the subsequent period.

Due to its fast and strong impact of straightforwardly focusing on VEGF, intraocular bevacizumab was built up as a standard convention for NVG treatment (Sugimoto et al.,2010). Nonetheless, the majority of the patients who got intraocular bevacizumab required extra infusions, PRP, or in the long haul, careful treatment for IOP control (Wakabayashi et al.,2008; Bhagat et al.,2016; Kotecha et al.,2011). By and large, a medication with intracameral infusion shows shorter half-life and term of impact than those directed by means of intravitreal infusion. Nonetheless, intracameral infusion can be acted within the sight of media opacities, has less vitreoretinal confusions, and shows preferable IOP-bringing down impacts over intravitreal infusion in certain reports (Bhagat et al.,2016).

A few examinations for the utilization of intracameral bevacizumab have been directed in the ongoing years and others are as yet under preliminary to assess its part in the executives of NVG.

Contrasting our examinations and different investigations done, we found that the etiology of NVG was almost the equivalent. Gristani et al in 2006 utilized intracameral infusion bevacizumab according to 3 patients with auxiliary NVG due to PDR or ischemic CRVO (Gristani et al.,2006). Yuzbasioglu et al in 2009 played out their examination on NVG optional to PDR or CRVO. (Yuzbasioglu et al.,2009). Nonetheless, the method was unique; there was synchronous intravitreal and intracameral infusion. Bhojwani and Kelly in 2009 revealed an instance of NVG due to CRAO treated with a solitary ICB injection (Bhojwani et al.,2009).

Likewise there is study researched the drawn out adequacy and security of intracameral bevacizumab infusions and the prescient variables for inevitable IOP-bringing down surgery (Jun et al.,2017). With regards to the outcomes, there were incredible similitudes. Gristani et al in 2006 detailed abatement in spillage by IFA ahead of schedule as 1 day after injection. No irritation or backslide was seen inside the follow-up of about a month. Duch et al (2009) announced checked relapse of foremost fragment neovascularization with IOP control without separating medical procedure in 2 instances of the 6 infused in this study (Duch et al., 2009). Bhojwani and Kelly (2009) detailed relapse inside 48 hours of the infusion, and there was noteworthy decrease of IOP. In our investigation, 94% of our cases demonstrated neovascularization relapse in the fifth days, however dropped to 18% just in the primary month. Notwithstanding, there was gentle decrease in IOP during the entire follow up period. Wolf and Burkhard (2011) revealed the IOP-bringing down impact of intracameral bevacizumab can be seen multi week after the infusion, yet is restricted to a time of around 3 weeks (Wolf and Burkhard, 2011) Notwithstanding, the quick and successful reaction to intracameral bevacizumab infusion opens a period window for extra medicines, which are regularly important.

CONCLUSION

NVG is a generally normal and genuine condition which happens because of iris neovascularization. The regular aetiopathological factor is extreme, diffuse and interminable retinal ischemia .The hypoxic retina produces vasoproliferative development factors in endeavor to revascularize hypoxic regions.

A portion of the customary strategies for the board of NVG incorporate panretinal photocoagulation to incite relapse of the new vessels, clinical treatment with skin and fundamental hypotensive specialists, or careful obstruction and cyclodestructive methodology in late stages for IOP and relief from discomfort.

Bevacizumab (Avastin, Genentech Inc., San Fransisco, California) is a recombinant monoclonal counter acting agent against VEGF. It has been utilized by ophthalmologists as an intravitreal specialist in treatment of proliferative neovascular eye maladies, especially for CNV and in ARMD.

This investigation is a planned and elucidating 30 eyes of 30 patients with rubeosis iridis optional to NVG were incorporated. In this examination, intraocular infusion was acted in a careful ward after effective sedative drops. Intracameral Bevacizumab infusion of 1mg (0.04ml) into the front chamber, trailed by remedy of oral acetazolamide 500mg tablets following the methodology. IFA discoveries have been dissected, alongside specular microscopy after the

system in a 5 days, multi month, 3months, and a half year follow up period.

As respects rubeosis, the investigation demonstrated that bevacizumab is substantially more touchy in (5 days and one month) in causing relapse of new vessels.

In this investigation IFA was utilized as a subsequent device to evaluate relapse of new vessels after intracameral infusion of bevacizumab. It was discovered that a solitary use of the medication caused an emotional decrease of spillage from rubeotic vessels. Notwithstanding, this impact was not dependable and return of new vessels happened 3 months after the fact in the vast majority of the cases. Another subsequent instrument utilized in this investigation was specular microscopy to survey the impact of ICB on corneal endothelium. It archived insignificant changes on the endothelial cell include in most of cases.

Taking everything into account, in spite of the fact that bevacizumab is indicating a promising technique as an adjunctive treatment of foremost fragment neovascularization and NVG, in any case; there is as yet a requirement for controlled imminent preliminaries to build up long haul security, viability, and dosing rules in retinal ischemia and NVG.

CONFLICT OF INTEREST

None

REFERENCES

1. Hayreh SS.(2007). Neovascular glaucoma. Prog Retin Eye Res;26(5):470-85.
2. Shazly TA, Latina MA.(2009). Neovascular glaucoma: etiology, diagnosis and prognosis. Semin Ophthalmol.;24(2):113–21
3. Albert DM, Jakobiec FA.(1999). Neovascular Glaucoma. In: Albert DM, Jakobiec FA, editors. Principles and practice of ophthalmology, Philadelphia: WB Saunders Publishers.
4. Bakri SJ, Snyder MR, Reid JM, Pulido JS, Singh RJ. (2007). Pharmacokinetics of intravitreal bevacizumab (Avastin). Ophthalmology. 114 :855-859.
5. Sasamoto Y, Oshima Y, Miki A, et al. (2012). Clinical outcomes and changes in aqueous vascular endothelial growth factor levels after intravitreal bevacizumab for iris neovascularization and neovascular glaucoma: a retrospective two-dose comparative study. J Ocul Pharmacol Ther ;28:41–48
6. Chen T, et al. (2007).The change of the level of the vascular endothelial growth factor in aqueous humor of patients with neovascular glaucoma before and after anterior retinal cryotherapy. Zhonghua Yan Ke Za Zhi. ;43(7) : 622–5.
7. Ehlers JP, Spirn MJ, Lam A, Sivalingam A, Samuel MA, Tasman W. (2008). Combination intravitreal bevacizumab/panretinal photocoagulation versus panretinal photocoagulation alone in the treatment of neovascular glaucoma. Retina; 28 :696-702.
8. Krohne TU, Eter N, Holz FG, Meyer CH. (2008).Intraocular pharmacokinetics of bevacizumab after a single intravitreal injection in humans. Am J Ophthalmol; 146 :508-512.
9. Lisa C. Olmos, M.D., M.B.A. and Richard K. Lee, M.D., (2011). Ph.D:Medical and Surgical Treatment of Neovascular Glaucoma, Int Ophthalmol Clin. ; 51(3): 27–36.
10. Sugimoto Y, Mochizuki H, Okumichi H, et al. (2010). Effect of intravitreal bevacizumab on iris vessels in neovascular glaucoma patients. Graefes Arch Clin Exp Ophthalmol. ;248:1601–1609.
11. Wakabayashi T, Oshima Y, Sakaguchi H, et al. (2008). Intravitreal bevacizumab to treat iris neovascularization and neovascular glaucoma secondary to ischemic retinal diseases in 41 consecutive cases. Ophthalmology; 115:1571–1580.
12. Bhagat PR, Agrawal KU, Tandel D. (2016). Study of the effect of injection bevacizumab through various routes in neovascular glaucoma. J Curr Glaucoma Pract.;10:39–48.
13. Kotecha A, Spratt A, Ogunbowale L, et al. (2011). Intravitreal bevacizumab in refractory neovascular glaucoma: a prospective, observational case series. Arch Ophthalmol.;129:145–150.
14. Gristani S,Sabine Biester, Swaantje Peters, Olcay Tatar, Focke Ziemssen, Karl Ulrich Bartz-Schmidt, and The Tubingen Bevacizumab Study Group.(2006). Intracameral Bevacizumab for Rubeosis Iridis. Am J Ophthalmol ;142:158-160.
15. Yuzbasioglu E, Artunay O, Rasier R, Sengul A, Bahcecioglu H. (2009). Simultaneous intravitreal and intracameral injection of bevacizumab (Avastin) in neovascular glaucoma. J Ocul Pharmacol Ther; 25(3):259-64.
16. Bhojwani Rajan, Kelly P Simon. (2009). Anterior chamber Bevacizumab for rubeotic glaucoma secondary to retinal artery occlusion. Artery Research. 3:122-123.
17. Jun Young Ha, Tae Hee Lee, Mi Sun Sung, and Sang Woo Park. (2017). Efficacy and Safety of Intracameral Bevacizumab for Treatment of Neovascular Glaucoma, Korean J Ophthalmol. ; 31(6): 538–547.
18. Duch Susana, Oscar Buchacra, Elena Milla, David Andreu, Jesu´s Tellez. (2009). Intracameral bevacizumab for NVG: A pilot study in 6 patients. J Glaucoma;18(2):140-143
19. Armin Wolf & Burkhard Von Jago,UIbig M. (2011). Christos Haritoglou Ophthalmologica.;226(2):51-6.

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