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Efficacy of a combination of conservative and surgical methods of treatment for neovaascular glaucoma associated with diabetic retinopathy and central or branch retinal vein occlusion

U. P. Sydorchuk , I. Ia. Novytskyy

Danylo Halytsky Lviv National Medical University

Lviv (Ukraine)

Background: *Neovascular glaucoma (NVG) is secondary glaucoma which is often resistant to medical therapy and may potentially lead to blindness.*

Purpose: *To assess the efficacy of a combination of conservative and surgical methods of treatment for NVG associated with proliferative diabetic retinopathy (PDR) and central or branch retinal vein occlusion (CRVO or BRVO).*

Material and Methods: *Fifty-six patients (68 eyes) with NVG were under our observation. These included 48 patients (60 eyes) with NVG associated with PDR and 8 patients (8 eyes) with NVG associated with CRVO or BRVO. The mean patient age was 64.0 ± 10.0 years. Group 1 (22 patients, 33 eyes) received hypotensive ocular hypotensive medication, retinal laser photocoagulation and intravitreal ranibizumab. In addition to the above treatment, group 2 (34 patients, 35 eyes) received filtration surgery. Of the 68 eyes, 24 received single ranibizumab 0.5 mg injection; 26 eyes, two to four injections, and 18 eyes, five or more injections.*

Results: *The treatment resulted in a partial reduction in iris neovascularization in 53/68 eyes, and total reduction, in 15/68 eyes. In a total sample of patients, the IOP reduced from 29.1 ± 7.9 mmHg at baseline to 20.4 ± 4.8 mmHg after treatment, and the mean number of IOP-lowering medications, from 2.1 ± 1.1 at baseline to 0.9 ± 0.9 after treatment.*

Conclusion: *The combination treatment for NVG was found to enable an IOP reduction of 29.9% and prevent a significant reduction in visual acuity in 85% of eyes with NVG.*

Keywords:

secondary neovascular glaucoma, retinal laser photocoagulation, intravitreal anti-VEGF injection, ranibizumab, glaucoma surgery, intraocular pressure

Introduction

Neovascular glaucoma (NVG) is glaucoma secondary to neovascularization of the iris and of the angle; it develops with the formation of neovascular membranes. The disease is accompanied by elevated intraocular pressure (IOP) and the development of glaucomatous optic neuropathy [1]. In addition, it is often refractory to medical therapy and can result in irreversible vision loss and blindness [2].

The disease most often develops in the presence of proliferative diabetic retinopathy (PDR) or central or branch retinal vein occlusion (CRVO or BRVO) which in turn leads to retinal ischemia/hypoxia and subsequent release of angiogenic factors [3], the most important of which is vascular endothelial growth factor (VEGF).

Angiogenesis is a process occurring naturally to form new blood vessels from a pre-existing vascular network, and it is common in organisms during growth and development. Clinical issues arise when the vasculature is extensively disturbed through trauma or disease, leading to a critical reduction in tissue supply with nutrients and oxygen [4]. VEGF not only promotes angiogenesis, but also causes pathological neovascularization [5].

Since angiogenesis plays an important role in the progression of various pathological conditions (e.g., NVG), angiogenesis inhibitors have been the focus of attention in numerous clinical studies [4, 6].

The management of NVG has two main components. The first component is reduction of the IOP by medical and surgical means. The second component is reduction of ischemic drive that induces formation of blood vessels. The mainstay of this treatment component is panretinal laser photocoagulation (PRLP) in diabetic retinopathy (DR) or focal photocoagulation of sites of retinal ischemia in CRVO or BRVO. If performed early during the neovascularization process, PRLP can induce the regression of both anterior and posterior segment neovascularization [7].

Recent studies have demonstrated that a combination of anti-VEGF treatment and PRLP potentially increases the success of filtration surgery for NVG, and prevents intraoperative hemorrhagic complications and postoperative obstruction of filtration pathways [8].

Many authors, however, believe that further research is required to find an optimal combination of anti-VEGF therapy and PRLP for NVG [1, 7].

The purpose of the study was to assess the efficacy of a combination of conservative and surgical methods of treatment for NVG associated with PDR, CRVO or BRVO.

Material and Methods

This prospective non-randomized cohort study was approved by the Ethics Committee of Lviv National Medical University (minutes no. 7 of October 26, 2020) and adhered to the Declaration of Helsinki.

The patients involved in clinical research were under our observation and treated at the Oculus medical center, the clinical home of the Department of Ophthalmology, Post-Graduate Education.

Informed consent was obtained from all patients involved in the study. Inclusion criteria were patients with NVG associated with PDR, CRVO or BRVO.

Patients with non-compensated diabetes or a history of previous glaucoma surgery were excluded.

Fifty-six patients (68 eyes) with NVG were under our observation. These included 48 patients (60 eyes) with NVG associated with PDR and 8 patients (8 eyes) with NVG associated with CRVO or BRVO. Type 1 diabetes mellitus was diagnosed in 14 patients, and type 2 diabetes mellitus, in 34 patients. The mean patient age was 64.0 ± 10.0 years, and of the 56 patients, 28 were females and 28 were males.

Patients were divided into two groups. Group 1 (22 patients, 33 eyes) received hypotensive ocular hypotensive medication, retinal laser photocoagulation and intravitreal ranibizumab. Since group 2 (24 patients, 35 eyes) had inadequate IOP control (> 26 mmHg) on maximal medical therapy, they received a glaucoma filtration surgery, either our modification of sinus trabeculectomy (STE) [9] (28 patients, 28 eyes) or EXPRESS shunt implant (6 patients, 7 eyes). Postoperatively, patients were administered a broad-spectrum antibiotic in combination with corticosteroid for 10 days, followed by corticosteroid monotherapy for 10 days.

Another indication for surgery was inadequate IOP control in patients who had received less-than-maximum IOP-lowering therapy due to intolerability of some ocular hypotensive agents. This group was formed because its patients were refractory to anti-VEGF therapy and retinal laser photocoagulation.

The mean patient age in groups 1 and 2 was 63.0 ± 11.0 years and 65.0 ± 10.0 years, respectively. Group 1 consisted of 10 males and 12 females, and group 2, 18 males and 16 females. In group 1, NVG associated with PDR developed in 16 patients (27 eyes), and NVG associated with CRVO or BRVO, in 6 patients (6 eyes). In group 2, NVG associated with PDR developed in 32 patients (33 eyes), and NVG associated with CRVO or BRVO, in 2 patients (2 eyes). The numbers of patients with type 1 and type 2 diabetes were 2 and 14, respectively, for groups 1, and 12 and 20, respectively, for group 2.

Patients underwent best-corrected visual acuity (BCVA) assessment, Maklakoff tonometry, anterior eye and fundus examination using slit lamp and wide-angle lens (Volk Digital Wide Field lens; Volk Optical, Mentor, OH), and gonioscopy with Goldmann three-mirror lens (Volk Optical).

NVG stages were as per Dubey and Pegu (2009) [10]:

Stage 1, rubeosis iridis (new iris vessels appear at the pupillary margin and at the iris root). The IOP is within the normal range.

Stage 2, open-angle neovascular glaucoma (new vessels in the angle). The IOP is raised.

Stage 3, angle-closure NVG (the fibrovascular membrane in the angle contracts, causing peripheral anterior synechiae (PAS) and, as these PAS coalesce, synechial angle closure occurs; eversion of the pupillary margin is common). The IOP is raised, and may become decompensated in the form of an acute attack of NVG.

Topical beta-adrenergic blockers (timolol and betaxolol), carboanhydrase inhibitors (dorzolamide and brinzolamide), prostaglandin analogs (bimatoprost, latanoptost, travoptost, tafluptost) or their combinations were used for reducing IOP. During observation, hypotensive therapy was corrected, if necessary.

All patients received intravitreal injections of ranibizumab at a dose of 0.5 mg (Lucentis, Novartis Pharma AG, Bazel, Switzerland) to inhibit neovascularization of the iris and angle. In order to achieve the maximum accuracy for determining the amount of the drug, the contents of the vial were diluted twice in distilled water, and the preparation was injected a volume of 0.1 mL. Corneal paracentesis with partial drainage of the anterior chamber aqueous fluid was performed in order to reduce elevated IOP (i.e., an IOP as high as 22 mmHg or higher).

Of the 68 eyes, 24 received one ranibizumab injection; 26 eyes, two to four injections, and 18 eyes, five or more injections, with the mean number of injections per eye being 2.82 ± 2.2.

In group 1, of the 33 eyes, 12 received one ranibizumab injection; 16 eyes, two to four injections, and 5 eyes, five or more injections, with the mean number of injections per eye beings 3.41 ± 2.84.

In group 2, patients received a ranibizumab injection 5-7 days before surgery to prevent intraoperative bleeding. In two cases with decompensated IOP, urgent glaucoma surgery was conducted the next day after corneal paracentesis with partial drainage of the anterior chamber aqueous fluid. In group 2, of the 35 eyes, 12 received one ranibizumab injection; 10 eyes, two to four injections, and 13 eyes, five or more injections, and with the mean number of injections per eye was 2.97 ± 2.36.

PRLP was performed in all eyes with PDR (n = 60), and focal retinal photocoagulation, in all eyes with CRVO or BRVO (n = 8).

In PRLP, a continuous-wave laser system was used to deliver 1200-1600 laser burns of 500 μm within one to three sessions. The retinal photocoagulation procedure was performed two weeks after injection and was repeated if required.

Closed vitrectomy (CVE) as a stand-alone procedure for PDR was performed in 10/60 eyes (particularly, in 5/27 eyes in group 1 and 5/33 eyes in group 2). Of note is that, prior to the current study, CVE for PDR was performed in 5/10 eyes (particularly, in 2/5 eyes in group 1 and 3/5 eyes in group 2).

Phacoemulsification with intraocular lens (IOL) implantation as a stand-alone procedure was performed in 30/68 eyes (particularly, in 14/33 eyes in group 1 and 16/35 eyes in group 2). Of note that, prior to the current study, phacoemulsification with IOL implantation was performed in 17/30 eyes (particularly, in 6/14 eyes in group 1 and 11/16 eyes in group 2).

A combination of closed vitrectomy for PDR with phacoemulsification with IOL implantation was performed in 18/60 eyes (particularly, in 8/27 eyes in group 1 and 10/33 eyes in group 2). Of note that, prior to the current study, CVE for PDR was performed in 12/18 eyes (particularly, in 2/8 eyes in group 1 and 10/10 eyes in group 2).

Patient characteristics and treatment measures performed before and throughout the study are presented in Table 1.

Our algorithm of treatment for NVG associated with DR, CRVO or BRVO is presented in Fig. 1.

Patients were examined at day 7 and month 1 after intravitreal injection. In addition, they were examined the next day and at day 7 and 1 month after glaucoma surgery or more frequently, if needed. Moreover, they were examined at month 3, month 6, month 9 and month 12 after surgery, to assess the efficacy of treatment. Follow-up duration ranged from 12 months to 23 months.

Our primary outcome measure was the reduction in IOP, and secondary outcome measures were number of IOP-lowering medications, reduction in iris neovascularization,

Table 1. Demographics and characteristics of patients with neovascular glaucoma and treatment measures performed before and throughout the study

Characteristics	Total patients, n=68	Group 1, n=33	Group 2, n=35
Mean age, years	64.0 ± 10.0	63.0 ± 11.0	65.0±10.0 p>0.05
Males/females	28/28	10/12	18/16
Intraocular pressure, mean ± SD	29.1 ± 7.9	26.4 ± 8.8	31.6 ±6.1 p<0.05
Number of IOP-lowering medications, mean ± SD	2.1 ± 1.1	1.7 ± 1.1	2.5±0.8 p<0.05
Visual acuity (LogMAR), mean ± SD	0.95 ± 0.55	0.94 ± 0.63	0.96±0.47 p>0,05
Cause of NVG, n: DR CRVO and BRVO	 60 8	 27 6	 33 2
Type 1 diabetes, number of patients Type 2 diabetes, number of patients	14 34	2 14	12 20
Stage of iris neovascularization: 1, n 2, n 3, n	 2 50 16	 1 26 6	 1 24 10
Previous history of eye surgery, n: Phaco + IOL CVE Phaco + IOL + CVE	 17 5 12	 6 2 2	 11 3 10
Previous history of retinal laser photocoagulation, n	21	7	14
Previous history of anti-VEGF treatment, n	18	5	13
Treatment throughout the study, n: Anti-VEGF Laser photocoagulation Phaco + IOL CVE Phaco + IOL + CVE	 50 47 13 5 6	 28 26 7 3 6	 22 21 6 2 0

Note: BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; CVE, closed vitrectomy; DR, diabetic retinopathy; IOP, intraocular pressure; n, number of eyes; phaco + IOL, phacoemulsification plus intraocular lens implantation; p, significance of difference between the two groups; VEGF, anti-vascular endothelial growth factor

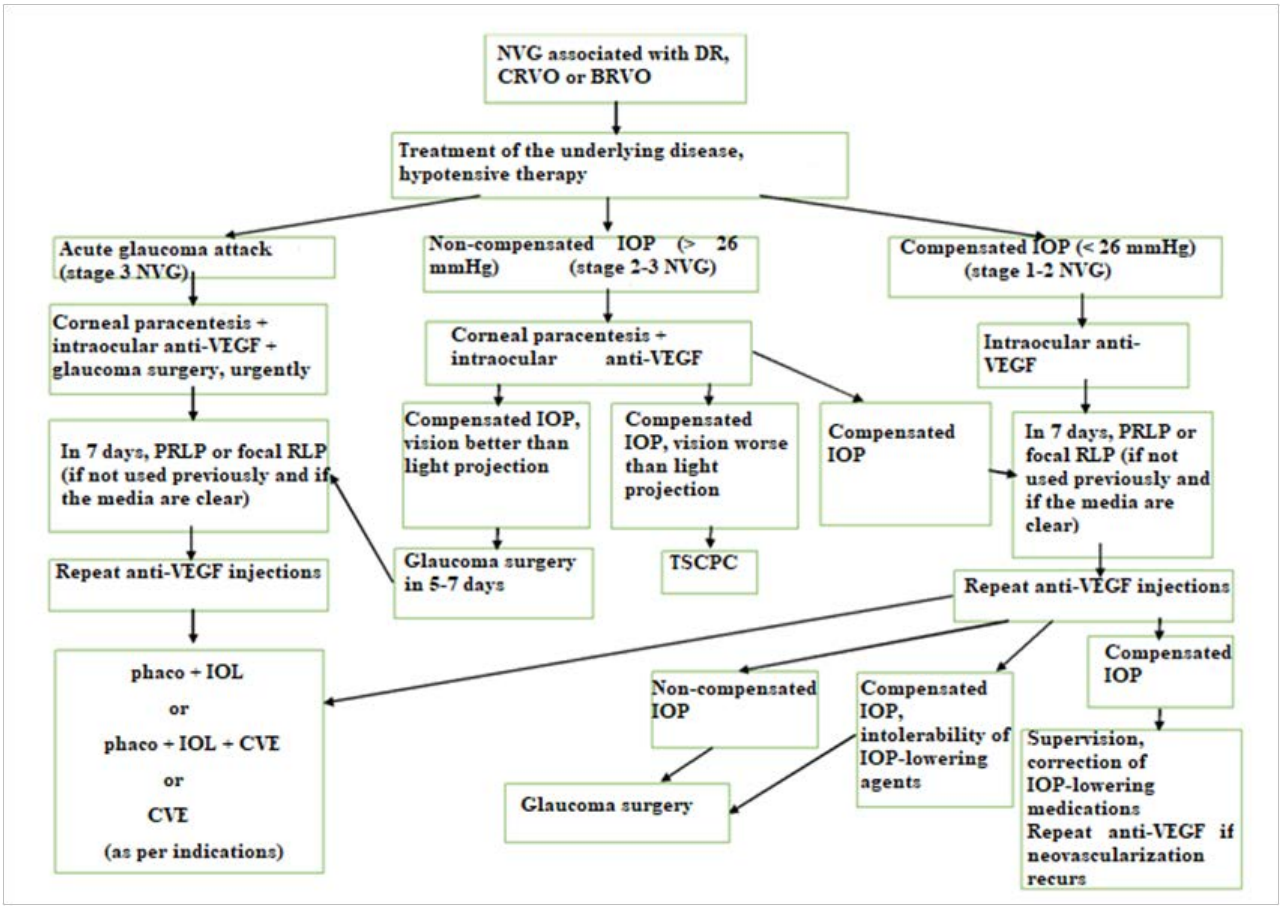

Fig. 1. Algorithm of treatment for NVG associated with DR, CRVO or BRVO.
Note: BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; CVE, closed vitrectomy; DR, diabetic retinopathy; IOP, intraocular pressure; phaco + IOL: phacoemulsification plus intraocular lens implantation; PRLP, panretinal laser photocoagulation; TSCPC, transscleral cyclophotocoagulation; VEGF, vascular endothelial growth factor

improvement in visual acuity, and type and number of postoperative complications.

MS Excel was used for statistical analysis. Data are presented as mean ± standard deviation (SD). Data were found to be normally distributed, and analyzed with a standard paired parametric t-test. A p value < 0.05 was considered significant for all comparisons. Visual acuity was converted to logarithm of the minimal angle of resolution (logMAR) for statistical analysis.

Results

Anterior segment biomicroscopy revealed pupillary margin neovascularization in all 56 patients (68 eyes). In addition, gonioscopy revealed neovascularization of the angle in 50/68 eyes and goniosynechiae in 16/68 eyes. Moreover, of these 16 eyes, 9 showed mydriasis and exhibited eversion of the pupillary margin (ectropion uveae).

NVG stage 1 was diagnosed in 2 patients (2 eyes; 2.9%), stage 2, in 41 patients (50 eyes, 73.5%), and stage 3, in 13 patients (16 eyes, 23.5%). Particularly, stages 1, 2 and 3 were diagnosed in 1 patient (1 eye; 3.0%), 18 patients (26 eyes, 78.8%), and 3 patients (6 eyes, 18.1%) in group 1, and 1 patient (1 eye; 2.9%), 23 patients (24 eyes, 68.6%), and 10 patients (10 eyes, 28.6%) in group 2.

No complications were noted after corneal paracentesis, intravitreal ranibizumab injection or retinal laser photocoagulation.

Three to five days after intravitreal ranibizumab injection, partial or total reduction in iris neovascularization (Figs. 2 and 3) and angle neovascularization (Figs 4 and 5) was noted in 53/68 eyes (77.9%) and 15/68 eyes (22.1%), respectively. There was, however, a difference between groups in treatment efficacy in terms of reduction in neovascularization: partial reduction in iris neovascularization and total reduction in neovascularization were observed in 26/33 eyes (78.8%) and 7/33 eyes (21.2%), respectively, in group 1, and 27/35 eyes (77.1%) and 8/35 eyes (22.9%), respectively, in group 2.

Hypotony and shallow anterior chamber due to overfiltration were noted after STE in 3/28 eyes (10.7%)

in group 2. A hyphema of less than 3 mm was revealed after STE and EXPRESS shunt implant in 4/28 eyes (14.3%) and 1/7 eyes (14.3%), respectively. In addition, signs of postoperative iridocyclitis were noted after STE and EXPRESS shunt implant in 6/28 eyes (21.4%) and 2/7 eyes (28.6%), respectively. Anterior chamber depth normalized, hyphema resolved and iridocyclitis relieved in the presence of standard anti-inflammatory therapy within a week after surgery.

Repeat procedures for glaucoma were performed in 2/28 eyes after STE and in 2/7 eyes after EXPRESS implant shunt at time points exceeding 6 months after initial surgery.

The IOP substantially and significantly reduced ($p < 0.05$) in both groups after treatment. In a total sample of patients with NVG associated with PDR, CRVO or BRVO, the IOP reduced by 29.9%, from 29.1 ± 7.9 mmHg at baseline to 20.4 ± 4.8 mmHg after treatment. Particularly, the IOP reduced by 19.7%, from 26.4 ± 8.8 mmHg at baseline to 20.9 ± 4.4 mmHg after treatment, in group 1, and by 37.0%, from 31.6 ± 6.1 mmHg at baseline to 19.9 ± 5.3 mmHg after treatment, in group 2. There was no significant difference in the IOP reduction after the procedure for glaucoma between eyes treated with STE and those treated with EXPRESS shunt implant. Mean IOP values for study groups at baseline and time points after treatment are presented in Fig. 6.

In a total sample of patients with NVG associated with PDR, CRVO or BRVO, the mean number of IOP-lowering medications reduced by 57.2%, from 2.1 ± 1.1 at baseline to 0.9 ± 0.9 after treatment. Particularly, the mean number of IOP-lowering medications reduced by 41.2%, from 1.7 ± 1.1 at baseline to 1.0 ± 1.0 after treatment, in group 1, and by 72.0%, from 2.5 ± 0.8 at baseline to 0.7 ± 0.8 after treatment, in group 2.

Over the follow-up period, the mean visual acuity in group 1 somewhat worsened from 0.94 ± 0.63 LogMar to 0.99 ± 0.63 LogMar, which may be explained by concomitant changes in the macular retina. In addition, in group 2, the mean visual acuity changed slightly, from 0.96 ± 0.47 LogMar to 0.97 ± 0.54 LogMar. Visual acuity was stable and practically did not change over the study period

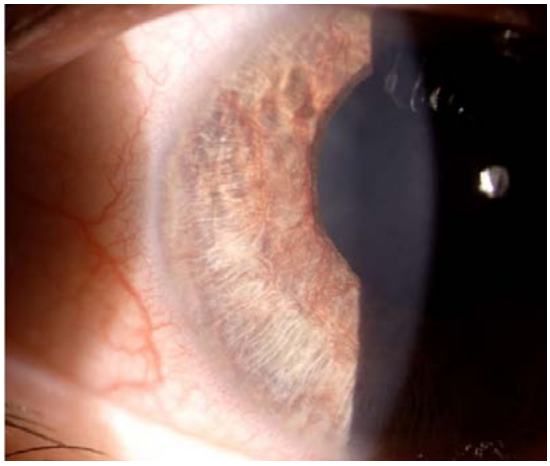

Fig. 2. Pre-treatment iris neovascularization in a patient with neovascular glaucoma

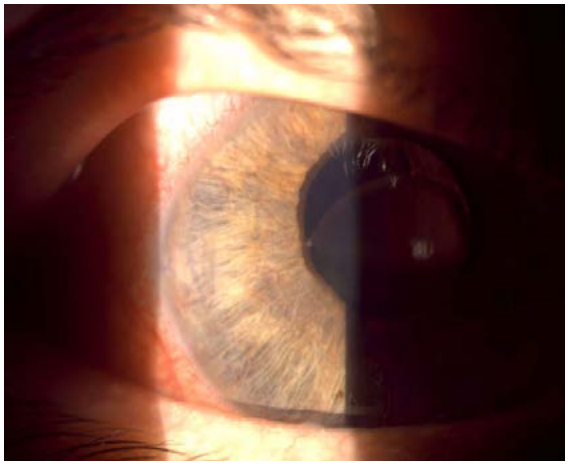

Fig. 3. Post-treatment partial reduction in iris neovascularization in a patient with neovascular glaucoma

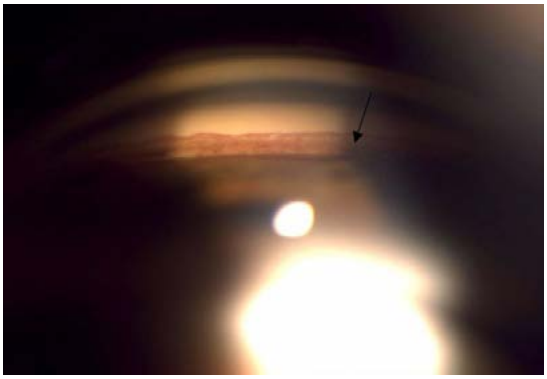

Fig. 4. Pre-treatment angle neovascularization in a patient with neovascular glaucoma (the arrow indicates trabecular neovascularization)

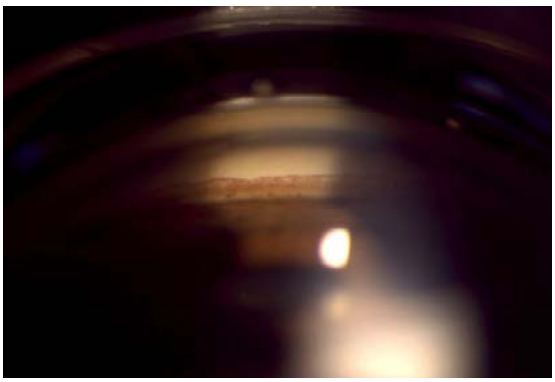

Fig. 5. Post-treatment total reduction in angle neovascularization in a patient with neovascular glaucoma

in a total sample of patients. There were no significant differences between groups in visual outcome. Therefore, our treatment resulted in the preservation of visual acuity in the majority (85%) of eyes in both groups.

Visual acuity (LogMar), IOP and numbers of IOP-lowering medications at baseline and after treatment for total patients and groups 1 and 2 are presented in Table 2.

Discussion

Recent clinical studies [11] on the use of intravitreal anti-VEGF medications in NVG demonstrated a reduction in neovascularization in the first 4-7 days and maintenance of IOP within normal limits in 60% of cases 3 months after injection.

Neovascularization of the iris typically begins at the papillary margin, and the formation of fibrovascular membranes in the angle cannot always be detected by gonioscopy. Therefore, anti-VEGF agents can help not only reduce iris neovascularization, but also prevent the formation of neovascular membranes in the angle [2, 11].

In the current study, all eyes with NVG exhibited a partial or total reduction in neovascularization of the iris and angle after intravitreal anti-VEGF injection and retinal laser photocoagulation.

Table 2. Mean pre- and post-treatment visual acuity, intraocular pressure (IOP), and number of IOP-lowering medications in groups of patients

Characteristic	Total patients, n = 68		Group 1, n = 33		Group 2, n = 35	
	Baseline	After treatment	Baseline	After treatment	Baseline	After treatment
Visual acuity, LogMar	0.95 ± 0.55	0.98 ± 0.58	0.94 ± 0.63	0.99 ± 0.63	0.96 ± 0.47	0.97 ± 0.54
p	p>0.05		p>0.05		p>0.05	
IOP, mmHg	29.1 ± 7.9	20.4 ± 4.8	26.48.8	20.9 ± 4.3	31.6 ± 6.1	19.9 ± 5.3
p	p<0.05		p<0.05		p<0.05	
Number of IOP-lowering medications	2.1 ± 1.1	0.9 ± 0.9	1.7 ± 1.1	1.0 ± 1.0	2.5 ± 0.8	0.7 ± 0.8
p	p<0.05		p<0.05		p<0.05	

Note: n, number of eyes; p, significance of value difference between pre-treatment and post-treatment;

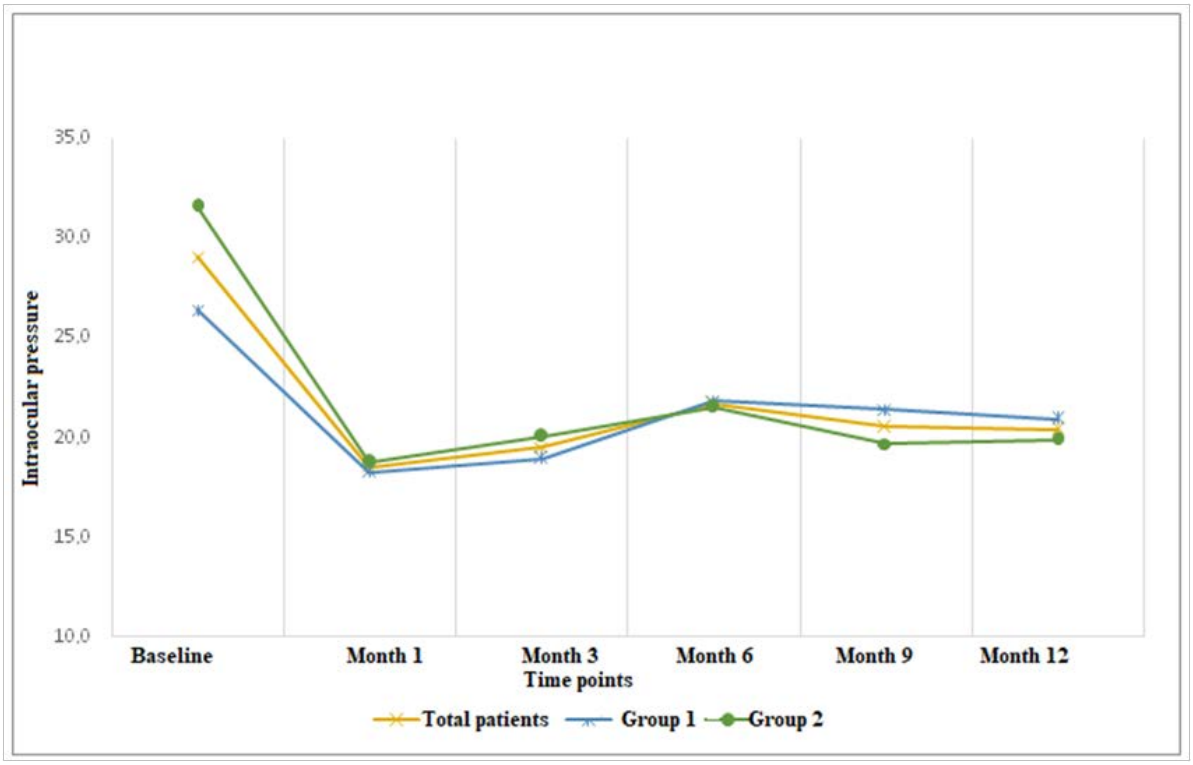

Fig. 6. Mean pre- and post-treatment intraocular pressure (mmHg) in groups of patients

A combination of intravitreal anti-VEGF with retinal laser photocoagulation was found to be more effective than intravitreal anti-VEGF only for the treatment and prevention of neovascularization in the anterior segment in patients with NVG, especially those with NVG associated with PDR [10].

Guidelines on the management of NVG associated with BRVO should be updated particularly with regard to the use of anti-VEGF medications. There is paucity of data on the optimal time for anti-VEGF therapy and retinal laser photocoagulation for preventing macular edema and neovascularization in the anterior segment in patients with NVG associated with BRVO or CRVO [12, 13].

Our findings demonstrate that a combination of retinal laser coagulation with anti-VEGF therapy is effective for stabilizing NVG associated with PDR, BRVO or CRVO, with a reduction in mean IOP from 26.4 ± 8 mmHg preoperatively to 20.9 ± 4.3 mmHg at 12 month in group 1.

Anti-VEGF therapy given in combination with retinal laser photocoagulation preoperatively has been beneficial in the management of NVG, primarily in terms of the rate of intraoperative in postoperative hemorrhagic complications and the degree of IOP compensation [14].

Our results demonstrate the efficacy of a combined approach to surgical treatment for NVG, with a reduction in mean IOP from 31.6 ± 6.1 mmHg preoperatively to 19.9 ± 5.3 mmHg at 12 month after conservative plus surgical treatment in group 2.

The current study is important since our complex treatment resulted in a 29.9% reduction in IOP, a 57.2% reduction in the number of IOP-lowering medications as well as the preservation of visual acuity.

Our results are in partial agreement with the results of a study by Al Rubaie and colleagues [14] who reported that their complex therapy contributed to the preservation of vision in 95% and compensation of IOP in 62% of cases.

There is a variety of NVG treatment algorithms which differ from each other in the sequence of components and indications for certain treatment options.

In the algorithm proposed by Tsai and Shields [15], attention is paid to whether pain is present or not, media are clear or not and whether neovascularization of the iris/angle is caused by inflammation or not. In addition, they have missed an important area of treatment, treatment of the underlying disease.

The scheme by Bai and colleagues [8] deserves attention. They proposed a therapeutic regimen including different approaches to different NVG stages, options for the type of anti-VEGF injection (intravitreal or intra-anterior chamber anti-VEGF injection), and a time window for anti-glaucoma surgery after anti-VEGF treatment. This scheme, however, does not mention the basic therapy for the underlying disease and opportunities and/or requirement for repeat anti-VEGF injections within the process of treatment (e.g., after surgery).

The NVG treatment algorithm by Rodrigues and Lim [16] considers the need for postoperative anti-VEGF injections. In this algorithm, however, the IOP level at presentation is not a defining factor for treatment strategy.

The NVG treatment algorithm by Sun and colleagues [13] is somewhat similar to ours. They introduce a combination of paracentesis of the anterior chamber and anti-VEGF injections in elevated IOP. Their algorithm, however, does not consider treatment in a blind, painful eye and does not emphasize the treatment of the disease underlying NVG [13].

The NVG treatment algorithm by Tang and colleagues [2] is the most similar to ours, but does not mention the basic therapy for the underlying disease and opportunities and/or requirement for repeat anti-VEGF injections within the process of treatment (e.g., after surgery).

In our NVG treatment algorithm, we have tried to overcome the shortcomings of previous algorithms and to propose the algorithm of measures, from the treatment of the underlying disease, hypotensive therapy, laser treatments, and intravitreal anti-VEGF injections, and ending with corneal paracentesis for elevated IOP, transition to surgical treatment with the use of all conservative treatment options during follow-up, and the use of surgery (phaco and closed vitrectomy) for restoration of transparency. Transscleral cyclophotocoagulation may be performed in a painful glaucoma eye with no useful vision (i.e., visual acuity worse than accurate projection of light).

Conclusion

Anti-VEGF therapy is effective in inhibiting neovascularization of the iris and angle, with partial and total reduction in iris neovascularization observed in 53/68 eyes and 15/68 eyes, respectively, observed at 5-7 days after anti-VEGF injection. A combination of retinal laser photocoagulation with anti-VEGF therapy is an effective tool for stabilizing NVG associated with PDR, BRVO or CRVO, with a reduction in mean IOP by 19.7%, from 26.4 ± 8 mmHg preoperatively to 20.9 ± 4.3 mmHg at the final follow-up visit, in group 1. The complex treatment for NVG includes IOP-lowering medications, retinal laser photocoagulation, anti-VEGF therapy, and an option of filtration surgery for eyes with non-compensated IOP; it was found to enable an IOP reduction of 29.9% and prevent a significant reduction in visual acuity in 85% of eyes with NVG. An algorithm of treatment for NVG associated with DR, CRVO or BRVO, which uses all currently available opportunities, has been proposed (Fig. 1).

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Corresponding Author: *Uliana P. Sydorchuk, Post-Graduate Student at Ophthalmology Department, Faculty of Post-Graduate Education, Danylo Halytsky Lviv National Medical University and Ophthalmologist at Oculus Medical Center, E-mail: ulianasem1120@gmail.com*

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Abbreviations: *Anti-VEGF, anti-vascular endothelial growth factor; BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; IOL, intraocular lens; IOP, intraocular pressure; NVG, neovascular glaucoma; PDR, proliferative diabetic retinopathy; PRLP, panretinal laser photocoagulation; STE, sinus trabeculectomy*