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Clinical Experience in the Management of Neovascular Glaucoma

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Background. Neovascular glaucoma (NVG) is a devastating ocular disease with poor prognosis. The ideal surgical procedure has yet to be determined. In this study, the clinical course and visual outcome of NVG and their fellow eyes were investigated and the most appropriate management was also evaluated.

Methods. The study was conducted retrospectively consisting of NVG in-patients of Taipei Veterans General Hospital who were under the care of the same glaucoma specialist between January, 1998 and September, 2000. All patients had a minimal follow-up period of 6 months.

Results. The total number of patients enrolled was 35 (number of eyes enrolled was 35) with mean age of 66.4 ± 12.3 years. The underlying cause was diabetes mellitus in 29 patients and central retinal vein occlusion in 6 patients. Twelve (34.3%) eyes had initial intraocular pressure (IOP) of over 60 mmHg. Only 1 (2.9%) eye had initial visual acuity better than 6/60. Four lesion eyes were able to receive panretinal photocoagulation whereas 31 eyes received panretinal cryotherapy. For IOP reducing procedures, 15 eyes received trabeculectomy, and 16 received Diode trans-scleral cyclophotocoagulation (TSCP). At the final visit, 20 eyes (trabeculectomy group: 11 and Diode TSCP group: 9) were able to maintain an IOP ≤ 21 mmHg. Of these eyes, 15 (trabeculectomy group: 8 and Diode TSCP group: 7) were able to maintain or improve their vision. Of the remaining 4 eyes, 2 had cyclocryotherapy and 2 had trabeculectomy followed by Diode TSCP. IOP were controlled in these 4 eyes but none were able to maintain stable vision. Among the 34 fellow eyes with stable IOP, 32 were able to maintain stable vision.

Conclusions. Trabeculectomy and Diode TSCP provided no statistically significant difference in IOP control ($p = 0.32$) and visual outcome ($p = 0.59$) in our patient group. More randomized, prospective trials are needed to define the most effective treatment for NVG.

Neovascular glaucoma (NVG) is the end result of a variety of ocular ischemic diseases.[1-5] Once the intractable final stage is developed, the eye often turns blind and painful with neovascularization of the iris (NVI), a very high intraocular pressure (IOP) and bullous keratopathy.[1-4] NVG follows a relentless course and has poor prognosis.[2] Despite the many advances in the treatment of NVG, the most effective option has not been determined. In this study, the clinical course and visual outcome of NVG as well as the most appropriate management in our population were investigated.

METHODS

The study was conducted retrospectively with chart review of newly diagnosed NVG inpatients of Taipei Veterans General Hospital between January, 1998 and September, 2000. All patients were under the care of the same glaucoma specialist and had a minimal follow-up period of 6 months.

NVG was diagnosed based on the findings of increased IOP (≥ 21 mmHg) with neovascularization on iris or on angle. Data collected included patients' age, sex, underlying ocular and systemic disease, best-cor-

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rected Snellen visual acuity (VA), intraocular pressure, slit lamp biomicroscopy, indirect ophthalmoscopy, fluorescein angiography finding as well as management at first visit and at each consecutive follow-up visit.

Lesion eye was defined as the eye most recently diagnosed as NVG regardless of the extent of NVI, neovascularization on angle, vitreous or retinal condition. If NVG occurred in both eyes, the eye with higher IOP was defined as the lesion eye.

Success of treatment was defined as an IOP ≤ 21 mmHg after follow-up of at least 6 months. Improvement of vision was defined as a difference of at least 1 category of VA (No light perception, Light perception to less than 1/60, 1/60-6/60, 6/30-6/15, 6/12-6/8.6, 6/7.5-6/6) between the initial visit and the last follow-up visit.

Statistical analysis for IOP control and visual outcome between trabeculectomy group and Diode transscleral cyclophotocoagulation (TSCP) group was evaluated using Chi-square test.

RESULTS

The total number of patients enrolled was 35 (22 males and 13 females). The mean age was 66.4 ± 12.3 years (range 34 to 86 years). The time of follow-up ranged from 6 months to 15 months, with a mean of 9 ± 2.5 months. The underlying cause of NVG was diabetes mellitus (DM) in 29 (82.8%) patients and central retinal vein occlusion (CRVO) in 6 (17.1%) patients.

Twenty-nine (82.8%) patients reported visual loss for 1 to 3 weeks before they sought any medical help. Of the 29 patients with NVG due to DM, 7 (24.1%) patients were not aware of their diabetic retinopathy. Because most of the cases presented with established NVG, the definite time of vascular occlusion or the time of onset of DM retinopathy could not be determined.

Lesion eye

Before the diagnosis of NVG, 10 (28.6%) lesion eyes had undergone panretinal photocoagulation (PRP). Six (17.1%) lesion eyes had cataract extractions and 3 (8.6%) had vitrectomies for proliferative diabetic retinopathy. None of these 3 patients had received PRP before the vitrectomies.

On presentation, only 1 (2.9%) lesion eye had initial VA of better than 6/60. One lesion (2.9%) eye had no light perception. Twelve (34.3%) lesion eyes had initial visual acuity of 1/60-6/60. The remaining 21(60.0%) eyes had VA of light perception to less than 1/60.

Nine (25.7%) eyes had initial IOP of 31-40 mmHg. Nine (25.7%) eyes were in the range of 41-50 mmHg. Five (14.3%) eyes were in the range from 51 to 60 mmHg and 12 (34.3%) eyes had initial IOP of above 60 mmHg.

For the treatment of retinal ischemic condition, 4 (11.4%) lesion eyes received PRP. Thirty-one (88.6%) lesion eyes received panretinal cryotherapy (PRC) because of cloudy media or small pupil. A 360 degree peritomy was performed and retinal cryoprobe was applied at -60 °C for about 7 to 12 seconds for each spot. Each quadrant received 3 rows of applications with 4 to 5 spots at each row. A total of 48 to 52 applications were applied in each eye.[6]

For IOP reducing procedures, 15 (42.9%) lesion eyes received trabeculectomy with mitomycin-C in which 1 patient (2.9%) received trabeculectomy twice. 0.02% mitomycin-C was soaked for 3 minutes under scleral flap for each trabeculectomy procedure. Sixteen (45.7%) patients had Diode TSCP. Two (5.7%) had cyclocryotherapy. Two patients had trabeculectomy with mitomycin-C followed by Diode TSCP later in the course of disease (Table 1).

At final visit, 24 (68.6%) lesion eyes were able to maintain an IOP not exceeding 21 mmHg. However,

Table 1. Final outcome of lesion eyes with different management

Management	Number of lesion eyes	Intraocular pressure ≤ 21 mmHg(%)	Vision stable or improved (%)
Trab	15	11 (73.3)	8 (53.3)
Diode TSCP	16	9 (56.3)	7 (43.7)
Cyclocryotherapy	2	2 (100.0)	0 (0.0)
Trab+Diode TSCP	2	2 (100.0)	0 (0.0)
p value[a]		0.32	0.59

Trab = trabeculectomy; TSCP = transcleral cyclophotocoagulation.

[a] Difference in intraocular pressure control and visual outcome was performed for trabeculectomy group and Diode TSCP group.

only 2 (5.7%) lesion eyes had improved vision. Thirteen (37.1%) lesion eyes were able to maintain stable vision and 20 (57.1%) eyes had deterioration of vision (Table 1). Five (14.3%) had deterioration of vision due to hypotony, 8 (22.9%) were due to uncontrolled IOP and 7 (20.0%) were because of the retinal condition. There was no significant difference in IOP control ($p = 0.32$) or visual outcome ($p = 0.59$) between trabeculectomy group and Diode TSCP group.

It was observed that 11 (31.4%) lesion eyes had complete regression of NVI and 21 (60.0%) lesion eyes had partial regression of NVI after 6 months of follow-up. Seven (63.6%) eyes with complete regression and 8 (38.1%) eyes with partial regression of NVI were able to maintain stable or improved vision. Eyes without any regression of NVI had deteriorated vision. Complete regression of NVI was found to associate with better visual outcomes (test for trend; $p = 0.04$).

Fellow eye

Of the 35 fellow eyes, 15 (42.9%) had initial best-corrected Snellen VA in the range from 6/15 to 6/6, and 34 (97.1%) of them had an initial IOP in the range of 11-20 mmHg. One had initial IOP of 37 mmHg on presentation.

One fellow eye had proliferative diabetic retinopathy with NVG. Twenty-eight eyes had nonproliferative diabetic retinopathy. PRP was applied to the fellow eye when retinal status approached high-risk nonproliferative diabetic retinopathy stage according to the Early Diabetic Retinopathy Study report.[3] One patient with NVG in both eyes received PRC due to hazy media. When CRVO is the underlying cause of the lesion eye, close observation of the fellow eye (6 eyes) is the rule.[1]

At the last follow-up, 34 (97.1%) fellow eyes were able to maintain an IOP no higher than 21 mmHg. One eye had an IOP over 30 mmHg. Thirty-two (91.4%) fellow eyes were able to maintain stable vision and 3 (8.6%) had deterioration of vision. One (2.9%) had worse vision because of NVG with uncontrolled IOP and 2 (5.7%) were due to diabetic retinopathy.

DISCUSSION

NVG is an end-stage complication of ischemic retinal vascular diseases. Only about 3% of cases of NVG are caused by ocular inflammation without retinal ischemia.[4] The goals of treatment of NVG is twofold: firstly, treatment of the underlying disease process and in most cases, the reduction of retinal ischemia and secondly, the reduction of IOP.

Reduction of ischemia is usually through retinal laser photocoagulation.[7-10] However, there are circumstances in which laser photocoagulation is not feasible, like dense cataract, vitreous hemorrhage, small pupil, *etc*. In these situations, transscleral panretinal cryotherapy is used to reduce ischemia and to abolish the neovascularization.[11-13] Studies on NVI regression rate by PRP varied from 33%-100%.[1,14] Striga and Ivanisevic reported that 1200 to 1600 spots of laser produced regression of rubeosis in 70.4% of diabetic patients.[14] An NVI regression rate of 60% was stated in Brooks' 32 cases in which NVG developed mostly due to CRVO.[1] In our series, NVI regressed in 75% of cases receiving PRP. The slight difference in the results may be explained by the differential distribution of underlying diseases as well as the small proportion of our cases receiving PRP.

On the other hand, an NVI regression rate of 94% by PRC in our series was comparable to the results of May's[12] and Sihota's[15] reports, and slightly higher than Brodell's 80%[11] and Mohan's 60% (3 out of 5 patients).[13] In Brodell's report, success of treatment diminished in 4 to 6 months despite an initial success rate of 90%. Long-term follow-up may reveal whether our population has the same treatment response.

Fernandez-Vigo *et al*. did not find any difference in the regression of rubeosis with PRC when compared with PRP.[16] The great difference in the number of our patients receiving PRP (4 cases) and PRC (31 cases) precluded a formal statistical comparison between the 2 treatment modalities.

Because our cases were those hospitalized in tertiary care center which reflected more refractory disease status, PRP or PRC with medication alone rarely caused normalization of IOP. Reduction of IOP could be attained by increasing outflow through filtering surgery or by decreasing inflow *via* cyclocryotherapy or cyclophotocoagulation.[2]

When the 2 cases receiving both trabeculectomy with mitomycin-C and Diode TSCP were excluded, we had a

73% success rate for IOP control with trabeculectomy. This result was better than Allen's 67% (16 of 24 eyes) in which no antimetabolite was used.[17] Comparable results were reported by Fernandez-Vigo who treated 20 diabetic NVG cases with PRP or PRC and conventional trabeculectomy.[16]

The number of our cases who received trabeculectomy and were able to maintain stable vision was comparable with that of Allen (54%)[17] but fewer than Flanagan's 100% (3 cases).[18] Preliminary photocoagulation was undertaken and 1 to 6 weeks was followed for regression of the neovascular element prior to trabeculectomy in Flanagan's cases.[18] The IOP was controlled and useful vision was maintained after a follow-up period of 5 months to 1 year. Our cases could rarely allow such time elapse because of uncontrollable IOP. In our population, we suspected that unsatisfactory visual preservation was mainly due to the rather late treatment. As stated previously, 82.8% of our patients suffered from visual loss for 1 to 3 weeks before any ophthalmic service was consulted. So, even though regression of NVI and adequate IOP control were attained in most cases, visual prognosis remained disappointing. Continual follow-up was required to assess the long-term success rate of trabeculectomy with mitomycin-C in our patients.

None of our patients receiving cyclocryotherapy were able to maintain stable vision. For the Diode TSCP group, vision remained stationary in 44% of patients. Bulbar atrophy occurred in 4 eyes, in which 1 had undergone PRC with cyclocryotherapy and 3 had undergone panretinal cryotherapy and Diode TSCP. It was reported that despite adequate IOP control, up to 70% of patients treated with cyclocryotherapy for refractory NVG would lose vision.[20] Although a lower complication rate by laser cyclophotocoagulation was reported, the percentage of patients with NVG who lose total vision with this modality remains high, with long-term vision loss of 46.6% reported by Shields and Shields.[21] From our results, trabeculectomy and Diode TSCP provided no statistically significant difference in final IOP control ($p = 0.32$) and visual outcomes ($p = 0.59$).

Fellow eyes of patients can often maintain stable vision through meticulous follow-up and prophylactic measures. Fellow eye of patients with CRVO has much better visual prognosis than the DM group.

Despite the many advances in the treatment of NVG, visual prognosis remains poor.[2] In our population, a substantial proportion of patients were not aware of their diabetic retinopathy. Routine ophthalmic screening and easily accessible follow-up systems for diabetic patients should be implemented as public health policies. Patient education about the possible ruinous ocular complications of diabetes and hypertension is important. More randomized prospective studies are required to draw a definite conclusion on the choice of surgical strategies that will provide optimal visual outcome.

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