ORIGINAL ARTICLE

Pan Retinal Photocoagulation VS Intravitreal Injection of Anti-VEGF in Treatment of Proliferative Diabetic Retinopathy

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Abstract

Background: ***Pan-retinal photocoagulation (PRP) was the standard treatment for reducing severe visual loss from proliferative diabetic retinopathy. PRP may damage the retina, resulting in peripheral vision loss or worsening diabetic macular edema (DME). Anti-VEGF was associated with superior visual acuity outcomes and fewer PDR-related complications.***

Aim: ***Pan-retinal photocoagulation (PRP) and intravitreal injection of anti-VEGF (Ranibizumab) were compared for their effectiveness in treating proliferative diabetic retinopathy (PDR).***

Patient and Methods: ***In this study, twenty eyes from twenty PDR sufferers were split into two groups. Ten cases in Group 1 received three intravitreal injections of anti-VEGF (Ranibizumab), and ten patients in Group 2 received pan-retinal photocoagulation (PRP) from the Al-Zahraa University Hospital outpatient clinic.***

Result: ***Based on how medication affected visual acuity, we found that cases receiving anti-VEGF had a significantly higher best-corrected distance visual acuity (BCDVA), with post-treatment BCDVA averaging 0.36±0.05 compared to the preoperative BCDVA of 0.25±0.07 (P ≤ 0.0008). On the other hand, in the Group treated by PRP, the BCDVA wasn't significantly improved (P>0.05), with post-treatment BCDVA averaging 0.29±0.17 compared to the preoperative BCDVA of 0.25±0.10. As regards the effect of treatment on neo-vessel regression, We observed substantial regression of new vessels in intravitreal anti-VEGF and PRP (60% and 70%, respectively) with minimal progression (20% and 10%, respectively), more prominently in the anti-VEGF Group, with a stationary course (20% and 20%, respectively).***

Conclusion: ***According to our research, anti-VEGF was linked to better visual acuity results and fewer problems from PDR. Additionally, it demonstrates that pan-retinal photocoagulation was not inferior to Ranibizumab in the treatment of PDR.***

Keywords: anti-VEGF (ranibizumab); PDR; FFA; PRP

1. Introduction

Long-term, poorly managed diabetes mellitus can culminate in diabetic retinopathy (DR), a microvascular disease that can harm the retina and, ultimately, blindness.[1]

It was among the most common preventable causes of blindness in adults of working age.[2]

DR often progresses in discrete, sequential stages, from moderate to non-proliferative diabetic retinopathy (NPDR) to PDR, which includes neovascularization of the retina and posterior vitreous surface.[3]

In individuals with type 1 diabetes (T1D) and type 2 diabetes (T2D), DR affects 77.3 percent and 25.1 percent of cases, respectively; about twenty-five to thirty percent of these cases go on to develop vision-threatening diabetic macular oedema. An increasing proportion of elderly individuals affected by diabetes and related comorbidities highlights the need for precise tracking of DR burden, evolution .[3]

Relative retinal ischemia creates a pro-angiogenic milieu in proliferative PDR, a microvascular disease. VEGF was a major mediator of angiogenesis.[4]

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Proliferative PDR was still typically treated with photocoagulation, but new FDA (Food & Drug Administration) approvals of Ranibizumab, aflibercept for the treatment of DME-related diabetic retinopathy may indicate that pharmacologic treatments of PDR may be possible.[5]

In newly diagnosed or refractory illnesses, intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF) can cause regression of diabetic neovascular complex, temporarily reducing leakage. Although the study was still in progress, clinical results show promise for continued use of anti-VEGF in proliferative diabetic retinopathy.[6]

In addition to PRP, anti-vascular endothelial growth factor (VEGF) drugs were a new therapeutic option. Anti-VEGF medications were linked to a decline in peripheral vision, loss of eyesight, and a lower incidence of central diabetic macular edema. For individuals with severe diabetic macular oedema, they were therefore thought to be a superior treatment to PRP. For PDR, three anti-VEGF medications were now being used: aflibercept, Ranibizumab, and bevacizumab. The effectiveness of each of these agents was thought to be roughly equivalent.[7]

The use of anti-VEGF carries dangers and restrictions. Floaters and a brief rise in intraocular pressure were frequent adverse effects. There have been reports of operator problems, including as severe intraocular damage to the lens. Endophthalmitis was rare; its incidence was thought to be 1 per 1000 injections.[8]

Our study aimed to Compare the effectiveness of pan-retinal photocoagulation (PRP) and intravitreal injection of anti-VEGF (Ranibizumab) in the treatment of proliferative diabetic retinopathy was the goal of our study.

2. Patients and methods

Twenty diabetic individuals with PDR in twenty eyes were included in this prospective interventional comparison. Split into two groups: Ten PDR cases receiving PRP were in Group 1, and ten PDR cases receiving three monthly intravitreal injections of anti-VEGF (Ranibizumab) were in Group 2. Prior to enrolment, all cases provided written informed consent to take part in the trial and to publish findings. The faculty of Medicine for Girls at Al-Azhar University in Cairo's Institutional Research Board (FMG-IRB) gave its approval to the study plan. Al-Zahraa University Hospital served as the study's location. Between January 2023 and October 2023, all cases were enrolled in the Department of Ophthalmology.

Exclusion criteria:

History of prior vitreoretinal surgery (vitrectomy, intravitreal triamcinolone injection) in the study eye.History of any thromboembolic event (including myocardial infarction or cerebral vascular accident). The presence of cataracts prevents optimal photography of the fundus.

Preoperative assessment

All subjects were subjected to the following: History taking including Name, age, sex,

medical history (underlying disease, duration and medications), and history of cataract or glaucoma. Complete ophthalmic examination including visual acuity (VA) uncorrected, best-corrected visual acuity (BCVA), values were converted to decimal for statistical analysis. Refraction using autorefractometer (Nidek ARK510A, Japan).

, IOP measurement (by Goldman applanation tonometer)(Keeler, UK), Slit lamp biomicroscopy examination (Topcon, Tokyo, Japan) for anterior segment examination, the iris for neovascularization, and the lens for the presence of cataract or pseudophakia Fundus examination (slit lamp biomicroscope with +90D volk lens and indirect ophthalmoscope). The presence of retinal neovascularization was assessed to identify cases with PDR. Fundus photo documentation degree of retinopathy and neo-vessel.

Fundus Fluorescein angiography.

Intravitreal injection of Ranibizumab

Every month for three months, 0.05 mL of ranizumab (Lucentis) was administered intravitreally via pars plana in a totally sterile environment.

We injected Superotemporally or inferotemporal for ease of access, though any quadrant can be used.

All patients received intravitreal injections in the operating theatre under complete aseptic conditions.

Pan-Retinal Photocoagulation

Pan-retinal photocoagulation was performed using laser photocoagulation systems with a green laser (GYC-500 NIDEK Gamagori, Aichi443-0038, JAPAN). Photocoagulation was performed by a retinal specialist in four sessions, with intervals of 1 -2 weeks between each session under topical anesthesia; spot size was set at 350 microns using a Mainster wide field lens, and each eye was subjected to 1300–1500 burns, and duration and power was adjusted to 0.02 and 300–500 mW, respectively, and PRP was applied in all 4 peripheral quadrants.

Postoperative evaluation:

All patients were examined postoperatively to exclude any complications, and the intra-ocular

pressure (IOP) was measured.

All patients were monitored one month postoperatively, during which a comprehensive ophthalmological assessment was conducted, focusing specifically on IOP and biomicroscopic assessment of the anterior segment to identify any alterations or problems. A fundus examination was conducted to identify changes following the injection. Fundus photo and Fundus Fluorescein Angiography were performed. Three months later, after the third injection or complete PRP sessions, a full ophthalmological examination was done.

Statistical Methods

Data analysis was carried out with MedCalc V. 20.110 software. P-value f01•m was used to evaluate the results' significance, which was classified as significant when the P-value was 0.05 and non-significant when the P-value > 0.05.

3. Results

Group 1 included ten cases two man (twenty percent%) & eight woman (eighty%) with mean ages 58.10±6.72 years and ranging from 50 to 67 years, and group 2 included 10 pt six man (sixty percent) , four woman (forty percent) with mean age 59.10±3.30 years and ranged from 55 to 64 years.

Regarding medical history, Group 1 included 7 cases that had IDDM (70%), 3 NIDDM (30%), 3 HTN (30%), and 4 had cataract surgery (40%). Group 2 included, 5 cases that had IDDM (50%), 5 NIDDM (50%), 5 HTN (50%), and 4 had cataract surgery (40%) No significant difference was found between 2 groups regarding age, sex, and medical history (P>0.05).

Visual acuity

Comparing mean BCDVA between the two groups showed insignificant difference between group 1 and group 2 preoperatively (0.25±0.07, 0.25±0.10 respectively) while postoperatively (0.36±0.05, 0.29±0.17 respectively) (P.>0.05). On the other hand, within group 1, BCVA showed a significant increase postoperatively (0.36±0.05) in comparison to preoperative BCDVA (0.25±0.07) (P ≤0.05). Group 2 showed no significant difference between pre and postoperative BCDVA (P>0.05).

Intraocular pressure

Comparing the mean IOP between the two groups showed an insignificant difference between group 1 and group 2 preoperatively (15±0.94,15.60+1.50 respectively) and postoperatively (16.20±1.13,16.60±0.96 respectively) (P > 0.05).

On the other hand, within group 1, postoperative IOP was significantly higher than preoperative IOP (P ≤ 0.05).

New vessels regression

Comparing postoperative new vessels regression between two groups showed an insignificant difference between group 1 and group 2 regarding incidence of regression (60%,70% respectively) progression (20%,10% respectively) and stationary course (20%, 20% respectively) (P.>0.05). Within group 1, no significant difference, while in group 2, 70% of cases significantly regressed (P ≤ 0.05).

Table 1. Demographic data of study group

Demographic data		**Group 1** (n=10)	**Group 2** (n=10)	**P.value**
Males	N (%)	2 (20%)	6 (60%)	0.0752
Females	N (%)	8 (80%)	4 (40%)	
Age (y)	Mean ± SD	58.10±6.72	59.30±3.16	0.616
	Range	50-67	55-64	
Medical history	IDDM	7 (70%)	5 (50%)	0.7468
	NIDDM	3(30%)	5 (50%)	
	HTN	3 (30%)	5 (50%)	
	Cataract surgery	4 (40%)	4 (40%)	

Table 2. Comparing BCDVA

BCVA	GROUP 1		GROUP 2		P.VALUE
	Mean	SD	Mean	SD	
PRE	0.25	0.07	0.25	0.1	1.000
POST	0.36	0.05	0.29	0.17	0.663
P.VALUE	0.0008*		0.5		

Table 3. Comparing IOP

IOP	GROUP 1		GROUP 2		P.VALUE
	Mean	SD	Mean	SD	
PRE	15.00	0.94	15.60	1.50	0.300
POST	16.20	1.13	16.60	0.96	0.407
P.VALUE	0.0188*		0.0927		

Table 4. Comparing postoperative new vessels between two groups

POSTOPERATIVE NEW VESSELS	GROUP 1		GROUP 2		CHI-SQUARE	P.VALUE
	N	%	N	%		
REGRESSION	6	60	7	70	0.209	0.6477
PROGRESSION	2	20	1	10	0.373	0.5416
STATIONARY	2	20	2	20	0.00	1.00
CHI SQUARE	6.200		6.400			
P.VALUE	0.2019		0.0450*			

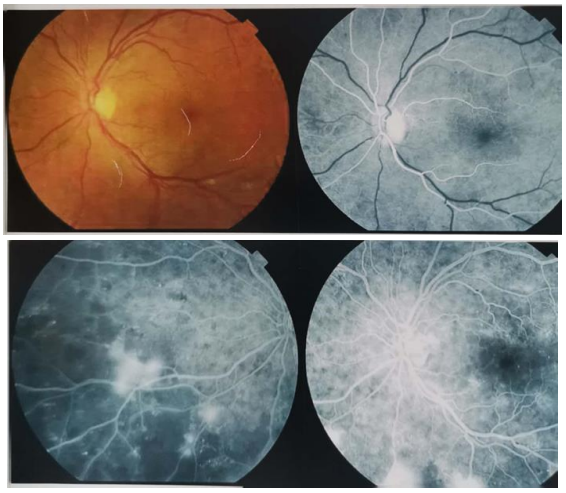

Figure 1. FFA of right eye of a case before P

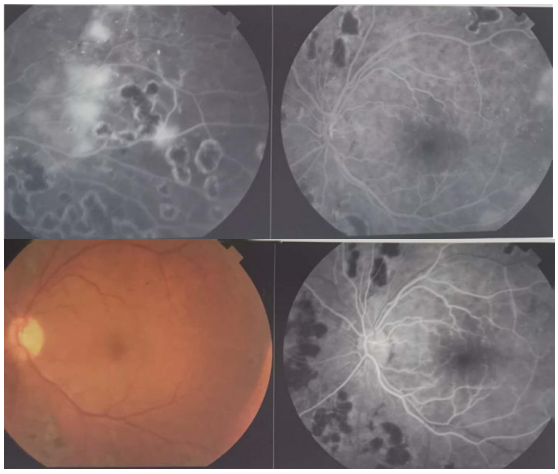

Figure 2. FFA of right eye of 1st case after PRP

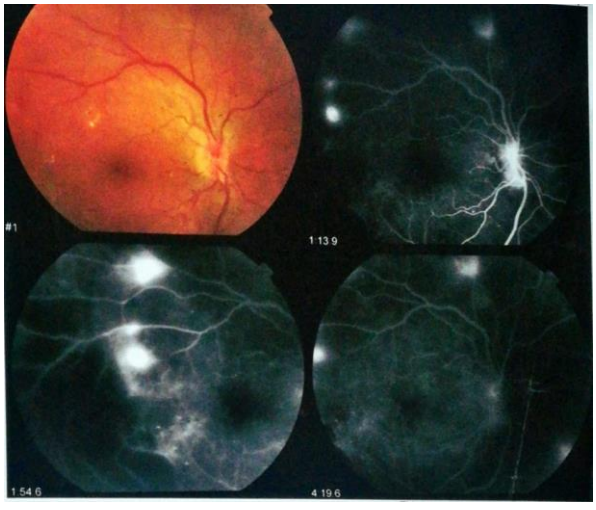

Figure 3. FFA of 3rd case of right eye before anti-VEGF

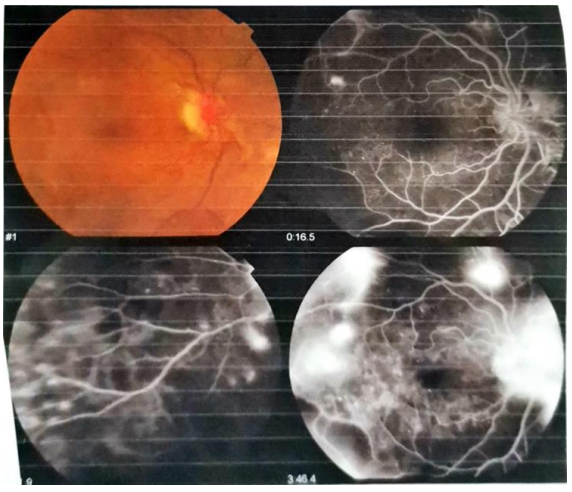

Figure 4. FFA of right eye of 3rd case after anti-VEGF

4. Discussion

Laser photocoagulation in a pan-retinal pattern, sometimes referred to as PRP, was the cornerstone of PDR treatment, causing neovascularisation to retreat. PRP raises oxygen tension in the eye and damages the ischaemic retina. 2 processes contribute to higher oxygen tension: greater diffusion of oxygen from the choroid in regions of photocoagulation scar nine and lower consumption from intentional retinal damage.[9]

In cases with newly diagnosed or refractory diabetes, intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF) can temporarily reduce leakage and induce regression of diabetic neovascular complex. Clinical results were encouraging for continued usage and applications of anti-VEGF in proliferative DR, even though research was still ongoing.[10]

In this study, we use FFA to diagnose PDR and evaluate the results of intravitreal injections of anti-VEGF against PRP.

Based on how medication affected visual acuity, we found that cases receiving anti-VEGF had a significantly higher best-corrected distance visual acuity (BCDVA), with post-treatment BCDVA averaging 0.36±0.05 compared to the preoperative BCDVA of 0.25±0.07 ($P \leq 0.0008$). On the other hand, in the Group treated by PRP, the BCDVA wasn't significantly improved ($P>0.05$), with post-treatment BCDVA averaging 0.25±0.1 compared to the preoperative BCDVA of 0.29±0.17.

In line with our findings, a CLARITY study conducted by Sivaprasad et al., demonstrated that intravitreal aflibercept monotherapy outperformed conventional PRP treatment for PDR via fifty-two weeks of anti-VEGF aflibercept, which has been demonstrated to produce quick improvements in visual acuity in short-term treatment of PDR.[11]

Additionally, a network meta-analysis (NMA) by Fallico et al. compared the treatment of PDR by anti-VEGF & PRP; both groups demonstrated better visual outcomes than PRP [anti-VEGF vs. PRP, mean difference (MD) = 3.42; standard error (SE) = 1.5; combined vs. PRP, MD = 3.92; SE = 1.65], with no difference between combined Group & anti-VEGF (MD = -0.50; SE = 1.87). PRP and anti-VEGF, either by themselves or in conjunction with PRP, did not differ in their ability to reduce neovascularization. However, there was a notable discrepancy (p = 0.016). The twelve-month visual outcomes for cases without DME did not differ across the 3 therapies; there was a significant discrepancy (p = 0.005) in the subgroup analysis.[12]

In contrast, Gross et al. showed that the ranibizumab group experienced an average (SD) change in visual acuity letter score of 3.1 (14.3) letters, while the PRP group experienced an average (SD) change of 3.0 (10.5) letters (adjusted difference, 0.6; 95 percent CI, −2.3 to 3.5; P =.68). After five years, average visual acuity for both groups was roughly 20/25 (Snellen equivalent). This discrepancy was caused by the shorter follow-up period of our study than the longer follow-up period.[13]

As regards the effect of treatment on IOP, mean intraocular pressure (IOP) before the injection of Ranibizumab was 15±0.94 mmHg, and it increased to 16.20 ± 1.1 mmHg after the injection. The mean difference was calculated to be1.20±0.19 mmHg, which was statistically significant (P ≤0.05). There was a slight increase in IOP following the third injection of Ranibizumab, aligning with findings by Bressler et al., who demonstrated that repeated I/V injections of Ranibizumab were related to a higher likelihood of sustained IOP elevation compared to laser treatment.[14] According to Leleu et al., the incidence of the last elevated IOP associated with I/V anti-VEGF injections is approximately 10%; this risk increases with the number of injections due to a cumulative effect.[15]

Hoguet et al.. Also, studies examining short-term intraocular pressure (IOP) increases (within 0 to 60 minutes post-intravitreal injection) consistently showed an immediate rise in IOP for all patients, with the elevation diminishing over time. Data on long-term IOP varied; according to seven studies, between four percent and fifteen percent of individuals had a persistent increase in IOP nine to twenty-four months after injection. Six investigations, in contrast, did not find any changes in IOP over the course of one to thirty-six months following injection.[16]

As regards the effect of treatment on neo-vessel regression, We observed substantial regression of new vessels in intravitreal anti-VEGF and PRP (60% and 70%, respectively) with minimal progression (20% and 10%, respectively), more prominently in the anti-VEGF Group, with a stationary course (20% and 20%, respectively). Sun et al., One hundred ninety-one eyes were given ranibizumab injections every month for six months. Nineteen percent (thirty-five of 188) of eyes treated with Ranibizumab at one month had full resolution of neovascularisation, while another sixty percent (113) had improved. At six months, neovascularisation resolution was observed in fifty-two percent (eighty of 153), improvement in three percent (four), stability in thirty-seven percent (fifty-six), and worsening in eight percent (thirteen) compared to the last visit.[10]

And also Shimouchi et al., 2020study which involved twenty eyes with proliferative diabetic retinopathy (PDR), showed that all instances of neovascularization (NV) had regressed following PRP treatment.[17]

Bressler et al. and Gross et al. studies demonstrated that for the treatment of PDR, Ranibizumab was not less effective than pan-retinal photocoagulation .[13,18]

4. Conclusion

Our research indicates that anti-VEGF was linked to better visual acuity results. It shows that pan-retinal photocoagulation was not inferior to Ranibizumab in the treatment of PDR.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article

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Conflicts of interest

There are no conflicts of interest.

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