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Proliferative Diabetic Retinopathy: A Review of Anti-VEGF Medications

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ABSTRACT:

"Vascular endothelial growth factor (VEGF)" has been linked to the development of diabetic retinopathy in earlier studies (DR). Although numerous research has examined the efficacy of "anti-VEGF for diabetic macular oedema", proliferative diabetic retinopathy has received less attention (PDR). This study is a review of pertinent works on the application of anti-VEGF to the management of PDR. "Systematic searches of PUBMED and the Cochrane Central Register of Controlled Trials" yielded the articles. We examined the strength of the scientific literature's evidence at the conclusion of each section. Anti-VEGF medications used off-label were proven to be helpful in PDR, particularly in situations of chronic vitreous haemorrhage, neovascular glaucoma, and preceding vitrectomy.

The use of "anti-VEGF" has drawbacks including short effect duration, rare occurrences of endophthalmitis, and tractional retinal detachment in cases with pre-existing pre-retinal fibrosis. Large randomised trials have not provided conclusive proof of the "effectiveness of anti-VEGF therapy in PDR". However, a number of case studies, a strong biochemical mechanism of action, and growing knowledge about the use of anti-VEGF medications can be utilised to support the continued use of this therapeutic approach in some patients.

INTRODUCTION:

One of the main causes of blindness is "proliferative diabetic retinopathy (PDR)". PDR affects roughly 1.5% of persons with diabetes. 1 According to the "Diabetic Retinopathy Study", around half of all PDR eyes that go untreated will experience severe vision loss ("visual acuity of o20/800 for at least 4 months"). [2]

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PDR is characterised by "vitreous haemorrhage and traction retinal detachment", as well as "retinal neovascularization, serum leakage, haemorrhage, and fibrovascular growth" in the vitreous retinal interface. [3] "Vascular endothelial growth factor (VEGF)", a pro-angiogenic cytokine, is thought to be the main cause of neovascularization in PDR. 4 Angiogenesis is at the core of PDR pathophysiology. 5 VEGF is a crucial participant in this process. 6,7 It has been noted that fibrovascular tissues and vitreous humour from eyes with PDR contain higher amounts of VEGF. "VEGFR-1 and VEGFR-2" are two tyrosine kinase receptors that VEGF activates. These receptors control both healthy and unhealthy angiogenesis.

Most vascular endothelial cells express VEGFR-2. 14 Similar to PDR, activation of VEGFR-2 promotes angiogenesis, microvascular permeability, endothelial cell migration, proliferation, and survival. [14] "Panretinal photocoagulation (PRP)" was the initial and only option for treating PDR until recently. The "Diabetic Retinopathy Study (DRS)" revealed a 450% drop in the rate of severe vision loss for PDR with high-risk characteristics when PRP was used. 15

The visual outcome typically turns out to be favourable when new vasculature reacts to PRP by regressing within the first three months after therapy.16 PRP had its own side effects, which included "pain during treatment, loss of peripheral vision, nyctalopia, uveal effusions, worsening of macular oedema, vitreous haemorrhage, and difficulty treating eyes" with vitreous haemorrhage, as well as advanced cataract,16–19 despite being proven to be beneficial. These issues necessitated the development of novel PDR treatment techniques, namely anti-VEGF. This review will provide a summary of the research on anti-VEGF therapy for PDR. Antı-VEGF drugs

1. "The US Food and Drug Administration has approved the use of bevacizumab (Avastin; Genentech, San Francisco, CA, USA), a full-length humanised anti-VEGF monoclonal antibody, for the treatment of colorectal cancer. 20 It is a big molecule with a twice longer half-life than ranibizumab (molecular weight: 148 kDa)". [21]

2. "Humanized, engineered recombinant antibody fragment (Fab) ranibizumab (Lucentis; Genentech USA, Inc., San Francisco, CA, USA/Novartis Ophthalmics, Basel, Switzerland) is effective against all VEGF-A isoforms. It has a shorter halflife than other anti-VEGF drugs and lacks the Fc domain. As an intravitreal agent for the treatment of wet, age-related macular degeneration, Lucentis is currently licenced (FDA approved) (AMD)".

MATERIALS AND METHODS:

Using electronic sources including "PUBMED and the Cochrane Central Register of Controlled Trials", the authors conducted thorough searches for published studies through August 2013 that assessed the impact of anti-VEGF medicines on PDR. The effects of anti-VEGF drugs for PDR therapy were looked up in the reference lists of selected studies and important review papers. Only articles in the English language were included in the search.

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"Proliferative diabetic retinopathy, retinal neovascularization, vitreous haemorrhage, neovascular glaucoma, anti-vascular endothelial growth factor, vascular endothelial growth factor, Macugen, pegaptanib, bevacizumab, Lucentis, and ranibizumab were some of the search phrases used". Before these results were drawn, the authors separately categorised the studies.

Additionally, relevant publications that were included as references in the retrieved articles were included. The removal of redundant research and publications deemed unrelated to PDR. Evidence levels are based on data from Australia's National Health and Medical Research Council.

Treatment for and safety of anti-VEGF Anti-VEGF medication dosage and frequency in PDR cases Bevacizumab's ideal dosage and administration method are still unknown. 1.25 mg has been utilised in the majority of investigations. 25–29 Garcia-Amaris and According to the treating clinician's judgement, Arevalo utilised bevacizumab dosages of 1.25 mg (20.5%) and 2.5 mg (79.5%), and found that the 2.5 mg dose was superior to the 1.25 mg dose for curing naive eyes' neovascularization completely.

A very et al.31,32, on the other hand, found no appreciable variations in the effects of bevacizumab at different doses, ranging "from 6.2 mg to 1.25 mg", on retinal neovascularization. They posited, however, that the longevity of the drug's effect might vary, with greater doses causing a longer-lasting effect. As a preoperative adjunct therapy for patients having "vitrectomy for PDR", Hattori et al. demonstrated that the lowest dose of intravitreal bevacizumab (IVB) tested (0.16 mg) was just as effective as the normal dose (1.25 mg). "The National Health and Medical Research Council" classification of research with supporting data Intervention Level I A thorough analysis of level II studies a controlled, random experiment

III-1 a pseudorandomized controlled trial (i.e., using a different allocation scheme or another approach)

III-2 Comparative research with ongoing controls: experimental study that wasn't random

Cohort research Case-control research

Time series with gaps and a control group III-3 a comparison without parallel controls study of historical controls at least two single-arm studies Time series with gaps and no corresponding control group IVB injections given repeatedly or at larger doses (2.5 mg) have been linked to an increase in the foveal avascular zone (FAZ), albeit this has not been proved (see below discussion).

The dosage of bevacizumab for these purposes is also not yet known. Re-injections were frequently reserved for situations where recurrence was plainly evident. Bevacizumab dose 1.25 mg's ability to reverse neovascularization: level IV evidence

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Retinal neovascularization regression and recurrence rates All anti-VEGF medications have demonstrated positive neovascularization regression results, although they were all constrained by their brief half-lives. None of the alternatives can match PRP's exceptional durability, which makes it the preferred method of treating PDR. Following anti-VEGF therapy, the typical time until retinal neovascularization returns ranges from 1 week27 to 3 months. A typical end point for assessing the efficacy of anti-VEGF therapy appears to be the persistence of the treatment's effects six months after injection.

"Unfortunately, only a few studies had a 6-month follow-up. In a prospective interventional case series on IVB in active PDR, five eyes had iris neovascularization (NVI) at the time of the baseline assessment, but only two still did one week later. There were no NVI cases discovered at week 6, but two cases, one of which was a recurrence and the other a new case, were discovered at week 12. 28 weeks after receiving bevacizumab treatment, 61.4% of patients showed complete regression without fluorescein leakage, 34% of patients showed a partial regression, and 4.5% of patients showed no regression of neovascularization, according to Arevalo and Garcia-Amaris [30]. Mendrinos et al. discovered that 1 year after a single injection of pegaptanib, neovascularization in a patient with prior PRP totally vanished. Adamis et al. found a potential permanent positive impact with intravitreal pegaptanib in a retrospective investigation of 16 patients with PDR, with 62% of the treated eyes (n=13) displaying regression or a lack of neovascularization at the 6-month follow-up visit. Although just one patient had high-risk PDR, the average number of injections was 5 (with a range of 3-6). In 15 injected eyes, Minnella et al. found that the bevacizumab's early effects lasted three months later. Schmidinger et al. noted that 62% (8 of 13) of the eyes required retreatment with bevacizumab at a 3-month checkup because new vessels had started to appear again. Total regression was seen in 87.5% of the eyes treated with Avastin injections and 25% of the sham group at week 6 of follow-up in Mishahi et al.28's investigation (Po0.005). Although the full regression rates in the two groups were identical (25%; P=1.000), PDR recurred in a sizable number of the eyes receiving Avastin treatment at week 16".

In conclusion, our investigations shown that intravitreal anti-VEGF can result in the regression of PDR-related neovascularization. Despite having a shorter duration than PRP, even a transitory effect may be advantageous in a number of clinical situations, such as when there is media opacity that prevents PRP from working, when rubeosis has not yet caused angle closure, or when used as a preoperative surgical adjuvant. "After one Avastin injection in a patient with PDR, there was an average rate of retinal neovascularization regression of 6 weeks and recurrence of 16 weeks: level of evidence II".

Bevacizumab can result in VEGF "Tractional Retinal Detachment (TRD)" in patients with severe PDR. This fibrous tissue's ability to contract can result in TRD and vitreous haemorrhage. Extreme variations in "intraocular pressure (IOP)" and the globe's distortion

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during intravitreal injection, which causes vitreoretinal traction, are two other hypothesised explanations.

"Longer time between bevacizumab injection and vitrectomy in patients with uncontrolled diabetes, vitreous haemorrhage, and PDR resistant to PRP are risk factors for TRD following bevacizumab.43,50 The use of the larger dose of IVB and the 413-day delay between IVB and vitrectomy were risk factors for TRD following IVB in a retrospective, multicenter, interventional, comparative case study on IVB for PDR (2.5 mg). Factors at risk for TRD following IVB in patients with PDR (degree of evidence III-2)":

Vitreous bleeding, KK PDR resistant to PRP, K 413-day window between IVB and vitrectomy, and K utilisation of greater IVB dose (2.5 mg).

FAZ enlargement: "Single case reports have described the development of retinal ischaemia after IVB. Following pars plana vitrectomy and therapy with 2.5mg bevacizumab, Lee and Koh documented angiographically an FAZ enlargement. However, in a prospective randomised, single-center 2-year trial comparing 1.25mg IVB (42 eyes) with laser therapy (38 eyes) in patients with diabetic macular edoema, retinal perfusion was evaluated. 53 The mean maximum linear dimension of the FAZ was 685262 microns in the laser group and 737262 microns in the bevacizumab group at baseline. At the 4-month time point (P140.40), there was no statistically significant difference. The mean maximum linear dimension of the FAZ was 678221 microns in the laser group and 678231 microns in the bevacizumab group". At 4 months, neither group showed any signs of deteriorating retinal ischaemia, it was determined. There is no evidence of macular ischaemia developing after IVB: level II evidence.Increase in IOP: Several mechanisms can account for the IOP increase that occurs after an intravitreal injection. An IOP spike is mostly caused by a transient rise in vitreous volume. Such a rise, according to studies using pegaptanib, normalises in 1 hour. Blockage of the trabecular meshwork by the big 148-kDa protein bevacizumab is one of the other potential causes of the increased IOP following IVB. After bevacizumab, transitory IOP rises were observed to occur 0.16% of the time.

IVB injection-induced temporary increase in IOP: level IV of evidence. Bevacizumab may result in macular retinal detachment, fast neovascular involution with accelerated fibrosis, posterior hyaloid contraction, and macular holes. Although macular hole can occur during the normal course of PDR or after vitrectomy alone, macular hole has been documented after bevacizumab in pars plana vitrectomy in diabetic eyes. Bevacizumab-induced macular hole development in diabetic patients: level IV evidence.

Other regional negative effects Uveitis is one of the additional side effects of bevacizumab and is most common at higher doses, with a reported prevalence of 0.09-1.9%.

Although endogenous VEGF plays a key role in the maintenance and survival of retinal neurons, Muller cells, and adult retinal photoreceptors, it has also been linked to pathological

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ocular neovascular disease. Long-term intravitreal anti-VEGF medications must be used carefully in this situation since they may harm these cells.

Risk of endophthalmitis per injection is between 0.05% and 1.2%; category II. Anti-VEGF side effects on the entire body Additional research is required to confirm the systemic side effects of anti-VEGF medications, particularly in diabetic individuals with serious vascular comorbidities. The most frequent systemic adverse effect is hypertension (for at least 6 weeks following the injection), which is followed by various cardiovascular issues. A retrospective analysis of 1173 patients who received IVB for DME and were monitored for 12 months now contains the largest data set for bevacizumab treatment. There were a number of negative outcomes documented, including 7 cases of acute blood pressure increase (0.4%), 6 strokes, 5 myocardial infarctions, and 5 fatalities. The rate of stroke was greater in the 0.5mg group (12 (4.8%) than in the 0.3mg group (5 (2.0%) or sham/0.5mg group (6 (2.4%) after 36 months of follow-up in the RISE and RIDE investigations on the efficacy of monthly 0.5 or 0.3mg ranibizumab or sham injection on DME patients. During month 36, there were 18 (7.2%) myocardial infarctions in the 0.3mg group and 9 (3.6%) in the 0.5mg group.

Systemic adverse events were similar in all three groups in the DRCRNet research, however there were 4 (4%) cardiovascular or cerebrovascular events in the sham group compared to 8 (7%) in the ranibizumab group and 4 (3%) in the triamcinolone group (P=0.33). There are larger data sets for AMD patients, however these patient populations are significantly distinct from one another clinically and demographically.

In contrast to the control group's incidence of 1.1%, patients receiving ranibizumab experienced higher rates of vascular events (2.1% myocardial infarction and stroke).

(Genentech Corporation, Lucentis (Ranibizumab injectable) Package Insert.) There were no systemic side effects recorded in the VISION study, which involved treating patients with neovascular AMD with intravitreal pegaptanib. With its low statistical ability to detect significant adverse events, the CATT Research Group examined ranibizumab and bevacizumab for neovascular AMD and found no differences in the rates of death, arteriothrombotic events, or venous thrombotic events. However, patients receiving bevacizumab experienced more significant systemic adverse events, predominantly hospitalizations, than patients receiving ranibizumab (24.1 vs. 19.0%, P=0.04). Conversely, Campbell et al. retrospectively examined population data and were unable to find an elevated risk.

However, younger diabetic patients who may have major vascular comorbidities may not be able to use these AMD data. Therefore, it is crucial to inform the patients about any potential systemic side effects of intravitreal anti-VEGF injections prior to the start of the treatment. Increased risk of elevation of blood pressure, stroke, andmyocardial infarctions after IVB in patient with DME: level of evidence IV.

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In NVG patients treated with intracameral bevacizumab, Lim et al. observed a large regression of iris neovascularization, a considerable decrease in intravitreal VEGF levels, and no appreciable changes in IOP during a 2-week period. Intractable glaucoma patients requiring shunt surgeries were shown by Eid et al. to have good success rates when PRP and bevacizumab were used to ablate the ischemic retina. In this trial, 10 eyes received bevacizumab injections one to two weeks prior to surgery, followed by PRP; 10 additional eyes served as the control group, receiving PRP alone preoperatively. In the bevacizumab and control groups, the mean IOP drops were 18.8 and 15.9mmHg over a 1-year follow-up, with success rates of 85 and 70%, respectively. It was hypothesised that the anti-VEGF therapy caused neovascularization to rapidly regress and created a therapeutic window of opportunity for the more lasting thermal laser ablation of ischemic retina.

Level of evidence III-3: Regression of iris neovascularization and no appreciable alterations in IOP in NVG patients treated with intracameral bevacizumab.

Vitreous haemorrhage (VH) is a frequent side effect of PDR. It is challenging to track the progression of the condition due to the opaque fundus, which may delay the treatment of potential retinal detachments or necessitate extra laser therapy.

Anti-VEGF medications speed up vitreous clear-up and lessen the need for vitrectomies.

Bevacizumab injections were typically given a week prior to vitrectomies in order to prevent TRD in the aforementioned severe PDR instances. The effectiveness of intravitreal ranibizumab was compared with intravitreal saline injections on vitrectomy rates for vitreous haemorrhage from PDR in a recent study by the Diabetic Retinopathy Clinical Research Network. In their investigation of 261 patients, the cumulative likelihood of vitrectomy by 16 weeks was found to be lower in both groups when ranibizumab was used (12%) compared to saline (17%). These results indicate that ranibizumab has little advantage over saline, and there was no comparator sham injection arm. The secondary outcomes imply that intravitreal ranibizumab may have a short-term biological advantage over intravitreal saline, including improved visual acuity, a decrease in recurrent vitreous haemorrhages, and a greater chance of successfully completing PRP. The risk of TRD was not observed to be higher. Level II evidence indicates that ranibizumab has little advantage over saline in preventing the need for vitrectomy in PDR patients with VH.

In PDR patients with VH, intravitreal ranibizumab has a short-term biological effect that improves visual acuity, reduces recurrent vitreous haemorrhages, and increases the likelihood that PRP will be completed.

In a another trial, Rizzo et al. randomly assigned 22 eyes with severe PDR and TRD to receive either IVB or a placebo injection 5-7 days prior to vitrectomy. They demonstrated that the bevacizumab group experienced fewer complications during surgery (which were measured by keeping track of operating times, tool swaps, number and severity of

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intraoperative bleeds, dissection procedures, and intraoperative retinal tears. Ahmadieh et al. enrolled 68 eyes that were going to get PDR vitrectomies. One week before to vitrectomy, they randomly assigned half to IVB and half to sham injection. The trial was only completed by 34 eyes because bevacizumab-treated individuals significantly improved following the injection. In the bevacizumab-treated group compared to the placebo group, intraoperative bleeding, post-vitrectomy haemorrhage, and the utilisation of intraoperative endodiathermy were all considerably lower. The results of the Cochrane study on anti-VEGF for PDR reveal that the rate of early (o3 weeks) POVCH is decreased following administration of preoperative IVB, and BCVA was improved 6 months after surgery. 81 Regarding the benefit of IVB on revision vitrectomy after 6 months and density of the POVCH, the data were unclear.

They discovered a little risk of TRD and elevated macular ischaemia in terms of negative effects.

The use of bevacizumab, in contrast, was found to be highly beneficial in a meta-analysis of six randomised controlled trials (published prior to the study by Ahn et al.) and one comparative study on the clinical outcomes of vitrectomy with or without IVB pre-treatment for severe diabetic retinopathy. The group that received IVB before surgery had a shorter surgical time (Po0.01). The IVB group's postoperative outcomes were significantly better than the control group's, with shorter blood absorption (P=0.04), significantly lower rates of recurrent VH (P=0.05), and improved final BCVA (P=0.003). Reoperation and complications, such as the eventual retinal detachment, were statistically negligible.

CONCLUSION:

In conclusion, the most current evidence suggests that preoperative IVB has a benefit for PDR, but bigger sample numbers and longer follow-up times are needed in randomised controlled trials to more accurately assess the long-term advantages and safety of bevacizumab pretreatment for severe PDR.

Level I evidence: IVB in eyes with PDR prior to vitrectomy decreased surgical time, postoperative vitreous cavity haemorrhage, and improved BCVA. IVB prior to vitrectomy decreased instrument exchanges, intraoperative bleeds (number and severity), dissection methods, and intraoperative retinal tears: level of evidence II.

“DME DME is frequently present in patients with PDR.Although PRP can lower the risk of severe vision loss in patients with high-risk PDR,17 there is a chance that macular oedema will worsen. The ETDRS findings show that scatter photocoagulation is ineffective for lowering the risk of mild vision loss in eyes with macular oedema, whereas focal photocoagulation is. In a phase 3 randomised, multicenter clinical trial, the Diabetic Retinopathy Clinical Network used 345 eyes with a visual acuity of 20/320 or higher, center-involved DME receiving focal/grid laser, and diabetic retinopathy receiving PRP. Patients

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were randomised to receive sham treatment, baseline and 4-week doses of 0.5 mg ranibizumab, or baseline and 4-week doses of 4 mg triamcinolone, respectively. In keeping with the findings for retinal thickness, mean improvements (SD) in visual acuity letter scores from baseline were substantially better in the ranibizumab (111; Po0.001) and triamcinolone (211; Po0.001) groups at the 14-week visit than in the sham group (414)". These results highlight ranibizumab's contribution to lowering the probability of short-term aggravation of macular edoema and related visual acuity loss after PRP. As the study was only intended to gather long-term safety data, not assess the efficacy of any medication beyond the 14-week study visit, these differences did not persist beyond 56 weeks. After receiving ranibizumab, endophthalmitis manifested in one eye (0.9%; 95% confidence interval, 0.02-4.7%). For patients with high-risk PDR, Filho et al. and Cho et al. compared PRP alone with PRP with ranibizumab or bevacizumab, respectively. In these investigations, the addition of ranibizumab/bevacizumab prevented the macular edoema that was seen in eyes that had only received PRP treatment. The likelihood of short-term worsening of macular edoema and related visual acuity loss was reduced in patients with DME receiving ranibizumab injection prior to PRP treatment: level II evidence.

PRP is presently the go-to treatment for PDR-active PDR that is resistant to PRP.

15 Despite the fact that PRP is effective at preventing NV and even causing it to regress in cases where it already exists, some cases of NV do not regress or even worsen in size,16 many people need additional laser therapy, and 4.5% require pars plana vitrectomy. In their research of 33 eyes from 24 patients with persistent NV in PDR following PRP, Erdol et al. discovered that complete resolution rates were "78.8% at 1 month, 63.6% at 3 months, and 45.4% at 6 months" with just one intravitreal injection of 1.25 of bevacizumab. After receiving 1.5 mg of IVB, diabetic individuals with actively leaking NV who were also resistant to PRP were followed up on for a year by Cintra et al. The BCVA in their study of 12 patients with persistent NV increased from baseline values of 0.900.11 to 0.700.12 at week 48 (P140.0449). The average number of injections given to subjects during the course of the 48-week research was 2.16. Mean fluorescein leakage was 27.76.2mm2 at baseline, and it significantly decreased at each subsequent visit following the injection (P140.0001). At week 6, there was no leakage.

Bevacizumab's effectiveness for eyes with active progressive PDR that are not responsive to PRP was assessed by Moradian et al. According to the procedure, bevacizumab was administered to 38 eyes at baseline and again after 6 or 12 weeks.

The resolution of the vitreous haemorrhage and regression of active fibrovascular tissue were regarded as the objectives. At 6 weeks, there was a significant vitreous haemorrhage resolution (P=0.06) but no meaningful impact on the fibrovascular tissue. As was already established, a negative side effect was that 5.3% of eyes developed TRD.

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In 15 eyes with persistent, active PDR, one injection of bevacizumab was given, according to Jorge et al. Fluorescein leakage was improved at the 12-week checkup, and there had been no serious adverse incidents. At all time intervals (1, 6 and 12 weeks), BCVA considerably improved from baseline, going from 20/160 at baseline to roughly 20/125 at 12 weeks. These investigations demonstrate that in persistent, active PDR, IVB reduces leakage from diabetic neovascular lesions.

For the purpose of converting these research findings into therapeutic recommendations, additional investigations are required, especially on long-term negative effects. Level of evidence III-2: Bevacizumab injection caused regression of persistent NV following PRP, improved BCVA, and reduced fluorescein leakage.

PDR (PRP) treatment combining anti-VEGF and traditional therapy has been documented in a few case series. For patients with high-risk PDR, Filho et al. 25–27 conducted prospective research comparing PRP alone to PRP with ranibizumab. In the first group, PRP was provided twice, while intravitreal ranibizumab was given to the second group after the first laser treatment. In comparison to PRP, intravitreal ranibizumab after PRP demonstrated a greater reduction in the overall area (mm2) of fluorescein leakage at week 48. However, the total area of actively leaking NVs was considerably decreased in the PRP plus IVB group compared to the PRP group at weeks 4, 9, and 16 in a study identical to Tonello et al.'s (Po0.001). Bevacizumab was given in this trial at the conclusion of the second laser session. IVB was studied by Cho et al. as an adjuvant therapy before PRP. IVB was injected 1 week prior to the start of PRP in his trial on 41 eyes of high-risk PDR patients. BCVA did not change in the PRP "Plus" group after 3 months, while it dramatically declined in the PRP group (P=0.041). When CME was present, neither group's BCVA significantly changed. In comparison to the PRP alone group, the number of eyes that experienced vitreous haemorrhage was considerably reduced in the "Plus" group (P=0.023).

In conclusion, intravitreal anti-VEGF has a significant positive impact on the management of high-risk PDR when combined with PRP.

Level of evidence III-3: Anti-VEGF administered following PRP therapy decreased fluorescein leakage in high-risk PDR.

The following scenarios are among the current indications for using anti-VEGF drugs in PDR:

(1) A week or less prior to the vitrectomy due to vitreous haemorrhage

(2) Neovascularization of the anterior section, preferably in those with an open angle.

(3) PDR and DME The short-term effects on reperfusion of aberrant arteries over time, TRD caused by fibrous contraction, and the uncommon risk of endophthalmitis are the drawbacks

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of anti-VEGF medications. 60 It's significant that PDR continues to utilise anti-VEGF medications off-label.

There are currently no significant, coordinated, randomised trials in this domain that provide high-level data. When the practitioner is aware of any potential side effects, the aforementioned information can be utilised as a justification to treat PDR in specific indications to enhance the patient's prognosis.

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