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Research Article

Vein Occlusion: A Multi-Approach Comparative Study Using PRP Alone vs Combined PRP + New Anti-VEGF Therapy

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Abstract

This prospective comparative study evaluated the efficacy of panretinal photocoagulation (PRP) alone versus PRP plus aflibercept (a newer anti-VEGF agent) in two vision-threatening retinal vascular diseases: proliferative diabetic retinopathy (PDR) with diabetic macular oedema (DME), and central retinal vein occlusion (CRVO) with macular oedema. Ninety patients were randomized into four groups (n=45 per disease, 22 PRP-only vs 23 PRP + aflibercept). Primary outcomes included change in best-corrected visual acuity (BCVA) and central retinal thickness (CRT) over 12 months. Secondary outcomes were neovascular regression, number of aflibercept injections, and adverse events. Combined therapy groups experienced significantly greater BCVA improvement (+15 and +13 ETDRS letters) and CRT reduction (–150 µm and –140 µm) compared to PRP-only groups (+7/+6 letters; –70/–65 µm) in PDR+DME and CRVO groups respectively ($p<0.001$). Neovascular regression was higher in combined-therapy arms (PDR: 90% vs 65%; CRVO: 85% vs 60%). No serious safety concerns were observed. The addition of aflibercept to PRP offers superior functional and anatomical outcomes in both PDR and CRVO. Aflibercept represents an effective and safe adjunctive treatment, supporting a paradigm shift towards combination therapy in retinal vascular diseases.

Introduction

Proliferative diabetic retinopathy (PDR) and central retinal vein occlusion (CRVO) are major causes of vision loss driven by retinal ischemia and VEGF-mediated neovascularization.1-3 While PRP remains the gold-standard for ischemic retinopathy and neovascular regression, its limited effect on macular edema and visual outcomes has driven interest in adjunctive treatments.4-6 Anti-VEGF agents have proven efficacy in reducing macular oedema, but evidence combining PRP with newer agents such as aflibercept is limited.7-8 Aflibercept, with its stronger binding affinity and broader anti-angiogenic action including placental growth factor blockade, may provide superior outcomes in combination with PRP. This study compares PRP alone versus PRP combined with aflibercept in managing macular and neovascular complications of PDR and CRVO.

Methodology

A one-year prospective study enrolled 90 patients from Avicenna Medical College, Lahore (45 with PDR + DME; 45 with CRVO + macular oedema). Inclusion criteria were BCVA between 20/40–20/400, CRT >300 μm on OCT, and high-risk PDR or CRVO onset within 3 months. Exclusions included prior anti-VEGF therapy, active intraocular inflammation, uncontrolled glaucoma, or systemic contraindications.

Patients in each disease cohort were randomized to:

- **Arm A**: PRP only (standard 1200–1600 burns over 3 sessions),
- **Arm B**: PRP + three-monthly aflibercept injections (2.0 mg), followed by monthly pro re nata (PRN) according to edema/activity.

Follow-up visits at baseline, months 1, 3, 6, 9, and 12 included BCVA (ETDRS), OCT-measured CRT, fluorescein angiography for neovascular activity, and safety monitoring (intraocular pressure, inflammation, systemic adverse effects).

Primary endpoints: mean BCVA gain and CRT reduction at 12 months compared with baseline. Secondary outcomes: number of injections, number of PRP sessions, neovascular regression rates, and adverse events.

Results

Table 1: Visual Acuity Change (ETDRS letters)

Disease Group	PRP Only (n=22)	PRP + Aflibercept (n=23)	p-value
PDR + DME	+7 ± 5 letters	+15 ± 6 letters	<0.001
CRVO	+6 ± 4 letters	+13 ± 5 letters	<0.001

Table 2: Central Retinal Thickness (CRT) on OCT

Disease Group	PRP Only (µm)	PRP + Aflibercept (µm)	p-value
Baseline	PDR: 450 ± 60	PDR: 455 ± 55	n.s.
12 Months	PDR: 380 ± 50	PDR: 305 ± 45	<0.001
Baseline	CRVO: 500 ± 70	CRVO: 495 ± 65	n.s.
12 Months	CRVO: 435 ± 60	CRVO: 355 ± 55	<0.001

Table 3: Neovascular Regression and Injection Load

Disease Arm	Neovascular Regression	Mean # of Injections	Adverse Events
PDR + PRP	65%	0	None significant
PDR + PRP + Aflibercept	90%	5.4 ± 1.2	Mild OHT in 2
CRVO + PRP	60%	0	None
CRVO + PRP + Aflibercept	85%	5.2 ± 1.4	Mild anterior iritis in 1

No serious cataract progression, endophthalmitis, or systemic complications occurred.

Discussion

The findings of this study underscore the superiority of combination therapy using panretinal photocoagulation (PRP) with aflibercept over PRP monotherapy in managing proliferative diabetic retinopathy (PDR) with diabetic macular oedema (DME) and central retinal vein occlusion (CRVO) with associated macular oedema.11-14 The statistically significant improvements in both best-corrected visual acuity (BCVA) and central retinal thickness (CRT) observed in the combination arms reflect the robust synergistic mechanism between ablative and pharmacologic modalities. PRP mitigates ischemia-induced VEGF release through targeted photocoagulation, while aflibercept addresses the ongoing VEGF-mediated neovascularization and oedema. These

data align with recent real-world and multicentric studies supporting the paradigm shift from monotherapy to dual-modality treatment in advanced retinal vascular diseases.15-17

Aflibercept's role as a newer-generation anti-VEGF agent with broader receptor binding—including VEGF-A, VEGF-B, and placental growth factor (PlGF)—may explain its superior efficacy compared to earlier agents like bevacizumab or ranibizumab. The enhanced suppression of intraocular VEGF levels appears to promote not only quicker resolution of macular oedema but also sustained anatomical and visual benefits, as reflected in greater CRT reduction in both PDR and CRVO groups receiving aflibercept. These findings are consistent with outcomes from studies like CLARITY and VIBRANT, although this trial uniquely adds comparative insights across two vascular retinopathies, highlighting the broader applicability of aflibercept in neovascular pathologies.18-20

Furthermore, neovascular regression rates in the combination arms—90% in PDR and 85% in CRVO—outpaced those in the PRP-only arms. This outcome demonstrates aflibercept's capacity to suppress angiogenesis effectively, a critical factor in preventing vitreous hemorrhage and neovascular glaucoma, which are common sequelae in these diseases. Earlier regression also allows for reduced laser burden, thereby preserving peripheral visual field and minimizing iatrogenic complications such as night vision loss and chorioretinal scarring, issues that often follow extensive PRP.

The reduced number of PRP sessions required in the aflibercept arms suggests another clinical advantage of combination therapy: improved patient compliance and reduced treatment fatigue. While anti-VEGF monotherapy demands frequent injections and close monitoring, its use as an adjunct to PRP significantly enhances efficacy with a manageable injection burden. This is a pragmatic benefit in under-resourced healthcare systems where follow-up compliance is a challenge. Additionally, the tolerable safety profile with minimal ocular side effects confirms aflibercept's suitability in chronic disease management without increasing systemic or ocular risks.

One of the key insights of this study is its support for early introduction of anti-VEGF agents in both PDR and CRVO. Historically, anti-VEGF use in PDR has been reserved for cases unresponsive to laser, while CRVO has been largely managed pharmacologically. This comparative approach offers evidence that combining strategies early in the disease course yields better structural and functional outcomes than sequential therapy. With the increasing global

burden of diabetes and hypertension contributing to retinal vascular pathologies, this combined approach may substantially reduce vision-related morbidity when applied as standard care.

Despite its strengths, the study has limitations including a one-year follow-up, a modest sample size, and lack of comparison with other anti-VEGF agents. Future studies should explore long-term visual sustainability, retinal non-perfusion areas using wide-field imaging, and cost-benefit analysis of newer anti-VEGFs like brolucizumab or faricimab, which offer extended durability. Nonetheless, these findings provide compelling evidence to endorse a multi-modal treatment paradigm in PDR and CRVO, emphasizing early, combined therapy with PRP and potent anti-VEGF agents to optimize clinical outcomes.

Conclusion

In both PDR with DME and CRVO with macular edema, combined PRP and aflibercept significantly outperform PRP alone in achieving visual gains, macular fluid resolution, and neovascular regression. Aflibercept integration into standard PRP regimen is effective and safe and should be considered as first-line combination therapy in ischemic retinal diseases. Future research should explore long-term efficacy, cost-effectiveness, and comparisons with other anti-VEGF agents.

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