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Intravitreal Steroid and Anti-VEGF in Macular Edema Secondary to Retinal Vein Occlusion

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SUMMARY

Aims: To evaluate the effectiveness and safety of combined intravitreal steroid and anti-VEGF treatment in patients with retinal vein occlusion at an ophthalmological referral center in Colombia.
Material and Methods: This is an analytical, longitudinal study of patients with macular edema secondary to retinal vein occlusion, who underwent treatment of combined intravitreal steroid and Anti-VEGF therapy at the Ophthalmology Department's Retina and Vitreous Unit, collected from an anonymized database.
Results: The study included 39 eyes from an anonymized secondary source, from January 2016 to December 2024. After an average follow-up of 18.7 months, a significant improvement in best-corrected visual acuity (from 1.22 to 0.93 LogMAR, p = 0.01) and a statistically significant reduction in central macular thickness (CMT) (from 567.5 to 236 µm, p = 0.01) were observed, with 76.9% of patients achieving a CMT < 300 µm. Intraocular pressure remained stable (15.18 vs. 15.69 mmHg). Most patients received Bevacizumab (64%) and Triamcinolone (66%), and 67% required intravitreal reinjections. The central retinal vein occlusion group showed visual improvement and a decrease in CMT, although 24% experienced complications, mainly elevated intraocular pressure and cataract progression. The superotemporal vein occlusion and inferotemporal vein occlusion groups also showed visual improvement and a reduction in CMT, with few complications.
Conclusion: Combination therapy was effective in improving visual function and reducing macular edema in different types of retinal vein occlusion.
Key words: retinal vein occlusion, macular edema, intravitreal injections, Ranibizumab, Aflibercept, Bevacizumab, Triamcinolone, Dexamethasone

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INTRODUCTION

Retinal vein occlusion (RVO) is the second most common cause of retinal vascular disease after diabetic retinopathy [1,2], affecting approximately 160,000 eyes each year, especially in patients over 65 years of age [3]. Anatomically, RVO is classified as central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO), with the majority (80%) corresponding to BRVO [4].

Among the primary complications associated with this pathology is macular edema, a significant cause of visual loss [5]. This develops in 5–15% of patients with BRVO within a year [6]. The treatments used for this complication include intravitreal steroids and anti-Vascular Endothelial Growth Factor agents (anti-VEGF) [7–9], which have proven effective, as evidenced by both visual acuity (VA) improvement and a decrease in central macular thickness (CMT) [7–9]. Although various studies have

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evaluated these groups of drugs as monotherapy, the effectiveness of combining these two therapies (intravitreal steroids plus anti-VEGF) has not been fully elucidated, nor has it been widely implemented in clinical practice. It has been demonstrated that early aggressive control of macular edema with a combined therapy may help prevent anatomical alterations caused by prolonged fluid accumulation that could lead to irreversible structural damage and consequent permanent visual dysfunction [10,11]. The purpose of this study is to evaluate the effectiveness and safety of combined treatment with intravitreal steroids and anti-VEGF in patients with macular edema secondary to retinal vein occlusion.

MATERIALS AND METHODS

This is an analytical, longitudinal study of patients with macular edema secondary to RVO who underwent intravitreal treatment with anti-VEGF at a monthly dose for 3 months, and a single dose of intravitreal steroid between the first and second month of anti-VEGF treatment at an Ophthalmology Department's Retina and Vitreous Unit in Floridablanca, Colombia. These data were collected from an anonymized database.

A total of 39 eyes from 39 patients between January 2016 and December 2024 were included. Patients with incomplete clinical records and patients diagnosed with macular diseases other than RVO were excluded from the study.

Sociodemographic variables of the sample were described by age and sex, and categorized according to type of RVO diagnosis. The following pre- and post-intervention variables were also evaluated: assessment of lens status, intraocular pressure (IOP) -mmHg-, best-corrected visual acuity (BCVA) -LogMAR-, CMT (microns), requirement for retinal laser during the treatment cycle, requirement for dual therapy intravitreal reinjections, as well as the number of injections, and postsurgical complications such as elevated IOP, cataract, or ocular hypotension.

Variables with normal distribution were described as means, with their respective standard deviations (SD). A description of the measures of central tendency and dispersion was performed, using the mean and standard deviation for normally distributed variables, and the median and interquartile range (IQR) for non-normally distributed variables. Qualitative variables were described using relative frequencies and absolute frequencies, with a 95% confidence interval. Bivariate analysis was performed by comparing results in each group, using Student's t-tests for dependent groups in normally distributed continuous variables and Wilcoxon tests for non-normally distributed variables, considering a p-value < 0.05 as statistically significant.

RESULTS

A total of 39 patients were included in the study, of whom 59% were men and 41% were women. The procedure was performed on a total of 39 eyes, corresponding to 18 right eyes and 21 left eyes. The patients included had an average age of 69 ±11.3, with ages ranging from 41 to 92 years. Of the 39 patients, two had previously had glaucoma; one was treated with Dorzolamide + Brimonidine + Timolol and Bimatoprost, and the other with Dorzolamide + Timolol. Prior to the intervention, the lens was assessed. Of the 39 eyes, 21 were found to have a transparent lens, 14 had cataracts, 4 were pseudophakic, and 0 were aphakic. The BCVA prior to surgery was 1.22 LogMAR ±0.68. Preoperative IOP was 15.18 mmHg ±3.13. The median preoperative CMT was 567.5 mc IQR 207. Regarding diagnosis, 29 patients were diagnosed with CRVO, 7 with ST-BRVO (Supero-temporal), and 3 with IT-BRVO (Infero-temporal) (Table 1).

All patients received intravitreal steroid therapy plus intravitreal anti-VEGF. Of the 39 patients, 25 received Bevacizumab, 4 received Ranibizumab, and 10 received Aflibercept. Of the 39 patients, 26 received Triamcinolone acetonide and 13 received a Dexamethasone implant. The median follow-up time was 8 months. During the dual therapy cycle, 7 patients received retinal laser therapy.

The average IOP after surgery was 15.69 mmHg ±3.93. On the other hand, the BCVA after intervention was 0.93 LogMAR ±0.68. In the post-intervention assessment of the lens, 41.10% of the lenses were found to be transparent, 48.7% had cataracts, 10% of the eyes were pseudophakic, and 0% were aphakic. The post-intervention CMT had a median of 236 µm with an interquartile range (IQR) of 81.

Among the 39 patients included in the study, 26 required intravitreal anti-VEGF reinjection, with a mean of 3.19 ±3.18 additional injections. Specifically, 8 patients received 1 additional injection, 3 patients required 2 injections, 11 patients required 3 injections, while 4 patients each required 4, 6, 11, and 15 additional injections, respectively. Regarding intravitreal corticosteroid therapy, re-implantation of Dexamethasone intravitreal implants was performed in 7 patients, with a mean of 1.7 ±1.25 additional implants. Of these, 5 patients required one

Table 1. Demographic and clinical characteristics of the population

Number of patients	Age (years)	Sex (M/F)	Eye (OS/OD)	Diagnosis			Pre-intervention lens status			
				CRVO	ST-BRVO	IT-BRVO	Clear	Cataract	Pseudophakic	Aphakic
39	69 ±11.3	23/16	21/18	74%	18%	8%	54%	36%	10%	0%

M – Male, F – Female, OS – Left eye, OD – Right eye, CRVO – Central retinal vein occlusion, ST-BRVO – Supero-temporal branch retinal vein occlusion, IT-BRVO – Infero-temporal branch retinal vein occlusion.

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Table 2. Patients with reinjection and mean number of reinjections (Mean ±SD)

Diagnosis	Dexamethasone implant		Triamcinolone		Anti VEGF	
	Reinjection	N° Reinjections	Reinjection	N° Reinjections	Reinjection	N° Reinjections
CVRO	AF: 6, RF: 0.20	1.83 ±1.32	AF: 2, RF: 0.06	1.50 ±0.71	AF: 20, RF: 0.76	3.3 ±3.5
ST-BRVO	NC	NC	AF: 1, RF: 0.14	2.00 ±0.0	AF: 4, RF: 0.15	2.75 ±2.36
IT-BRVO	AF: 1, RF: 0.33	3.00 ±0.00	NC	NC	AF: 2, RF: 0.076	3.0 ±3.0
GLOBAL	AF: 7, RF: 0.53	1.7 ±1.25	AF: 3, RF: 0.11	1.67 ±0.58	AF: 26, RF: 0.66	3.19 ±3.2

CRVO – Central retinal vein occlusion, ST-BRVO – Supero-temporal branch retinal vein occlusion, IT-BRVO – Infero-temporal branch retinal vein occlusion, AF – Absolute frequency, RF – Relative frequency, SD – Standard deviation, NC – No cases

additional implant, whereas one patient required three and one patient required four additional implants. In addition, Triamcinolone reinjection was administered in 3 patients, with a mean of 1.67 ±0.58 additional injections; one patient received a single reinjection and two patients required two reinjections. Notably, 7 patients received both anti-VEGF and steroid reinjections during follow-up. The median time interval between the completion of the initial treatment cycle and the reinjection date was 82.5 days (2.7 months). The reason for requiring re-intervention with anti-VEGF or steroids was the persistence of macular edema despite the initial treatment cycle (Table 2). All 26 patients received anti-VEGF reinjections until resolution of macular edema or loss to follow-up. In addition, combined therapy was reintroduced in patients presenting biomarkers associated with a favorable response to intravitreal corticosteroids, including subretinal fluid, disorganization of the retinal inner layers (DRIL), and cystoid macular edema (CME). This approach was also applied to patients with limited ability to attend regular follow-up visits, particularly those living in rural areas, as well as to patients who showed an insufficient response after multiple anti-VEGF reinjections.

An analysis of the differences in BCVA LogMAR before and after the intervention found an overall difference of 0.29 LogMAR VA in the sample. The associated p-value was < 0.05 (p = 0.01), indicating a statistically significant difference in the measurement of this variable before and after the intervention. With regard to the bivariate analysis performed to measure pre- and post-intervention CME using the Wilcoxon test, given the non-normal distribution of the data, a significant difference was found with a statistical significance level of alpha 0.05 (95% CI) (p = 0.01). Additionally, of the 39 patients, 30 patients (76.92%) obtained a CMT < 300 µm after the intervention.

The variable of admission diagnosis was categorized into three groups: CRVO, ST-BRVO and IT-BRVO.

In the CRVO group, pre-intervention BCVA was 1.34 LogMAR ±0.68 and post-intervention BCVA was 1.04 LogMAR ±0.68 (p = 0.03). The average pre-intervention intraocular pressure was 15.14 mmHg ±3.46, and the post-intervention average was 15.59 mmHg ±4.46. The pre-intervention CMT had a median of 578 µm with an interquartile range (IQR) of 184, while the post-intervention median for this variable was 236.5 µm with an interquartile range (IQR) of 84. A pre-intervention assessment of the lens was performed on the 29 patients, of whom 48.27% had a clear lens, 41.37% had cataracts, 10.34% had pseudophakia, and 0% had aphakia. After the intervention, 34.48% of the eyes in the group were found to have transparent lenses, 55.17% had cataracts, 10.34% had pseudophakia, and 0% had aphakia. During the intervention cycle, 13% of patients with this admission diagnosis received retinal laser treatment. Regarding complications in this group, of the 29 patients, 24.13% had complications, of which 17.24% were high IOP, with 2 of these patients also having cataract progression. Of the 29 patients, 6.89% had isolated cataract progression, and none had ocular hypotension.

Of the 39 patients, 7 belonged to the group diagnosed with ST-BRVO, where the BCVA pre-intervention was 0.98 LogMAR ±0.65, and the post-intervention BCVA was 0.81 LogMAR ±0.81. Regarding IOP behavior, the average pre-intervention IOP was 15.00 mmHg ±2.08, and the average post-intervention IOP was 16.14 mmHg ±1.68. The pre-intervention CMT had a median of 456 mc with an interquartile range (IQR) of 104.5, and the post-intervention CMT had a median of 229 µm with an interquartile range (IQR) of 63.5. Upon pre-intervention assessment of the lens in the 7 patients, 4 were found to have a transparent lens (57.14%), 2 had cataracts (28.57%), 1 had pseudophakia (14.28%), and 0 had aphakia upon post-intervention assessment, there were no changes in characteristics. Furthermore, 42% of the patients in this group received retinal laser treatment during the treatment cycle. Regarding complications, none of the patients in this group experienced complications.

The same variables were analyzed for the group diagnosed with IT-BRVO, which included three patients. Their BCVA before the intervention was 0.70 LogMAR ±0.26, and after the intervention it was 0.18 LogMAR ±0.00, meaning that all patients in this group had a favorable result with regard to BCVA after the intervention. With regard to IOP, the pre-intervention average was 16.00 mmHg ±2.00, and a slight decrease was found post-intervention, with an average of 15.67 mmHg ±2.52. CMT had a pre-intervention median of 785 µm with an interquartile range (IQR) of 212, and a post-intervention median of 256.5 µm with an IQR of 62, representing a significant decrease. When assessing the characteristics of

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Table 3. BCVA results (LogMAR), mean IOP (mmHg) ±SD. Median CMT (µm) IQR

Diagnosis	BCVA (LogMAR)			IOP (mmHg)		CMT (µm)	
	N	Pre	Post	Pre	Post	Pre	Post
CRVO	29	1.34 ±0.68 SD	1.04 ±0.68 SD	15.14 ±3.46 SD	15.59 ±4.46 SD	587 IQR 184	236.5 IQR 184
ST-BRVO	7	0.98 ±0.65 SD	0.81 ±0.81 SD	15.00 ±2.08 SD	16.14 ±1.68 SD	456 IQR 104.5	229 IQR 63.5
IT-BRVO	3	0.70 ±0.26 SD	0.18 ±0.00 SD	16.00 ±2.00 SD	15.67 ±2.52 SD	785 IQR 212	256.5 IQR 62
GLOBAL	39	1.22 ±0.68 SD	0.93 ±0.68 SD	15.18 ±3.13 SD	15.69 ±3.93 SD	567.5 IQR 207	236 IQR 81

CRVO – Central retinal vein occlusion, ST-BRVO – Supero-temporal branch retinal vein occlusion, IT-BRVO – Infero-temporal branch retinal vein occlusion, BCVA – Best corrected visual acuity (LogMAR), IOP – Intraocular pressure, CMT – Central macular thickness, SD – Standard deviation, IQR – Interquartile range

the lens, it was found that prior to the intervention, all patients in this group had a transparent lens. However, after the intervention, one patient (33.33% of the group) was found to have cataract, being the only complication described in this group. In addition, no patient in this group received retinal laser treatment during the treatment cycle.

The results of the variables evaluated and their behavior according to the groups established by the admission diagnosis are summarized in Table 3.

DISCUSSION

The present study evaluated the anatomical and functional outcomes of combined intravitreal corticosteroid and anti-VEGF therapy in patients with macular edema secondary to RVO, including both CRVO and BRVO subtypes. Our results demonstrated a statistically significant improvement in BCVA and a marked reduction in CMT following dual therapy, with stable IOP and a low incidence of adverse events.

The mean BCVA improved from 1.22 ±0.68 LogMAR to 0.93 ±0.68 LogMAR, and the median CMT decreased from 567.5 µm to 236 µm ($p < 0.01$). These outcomes are consistent with those reported in large randomized clinical trials of anti-VEGF monotherapy, such as the BRAVO and CRUISE studies, which demonstrated mean visual gains of approximately 14–18 ETDRS letters in BRVO and CRVO treated with Ranibizumab [12,13]. However, the degree of anatomical improvement observed in our cohort may reflect the synergistic action of the combined approach, as corticosteroids target inflammatory mediators and breakdown of the blood-retinal barrier, complementing the VEGF suppression provided by anti-VEGF agents [14]. This synergism has also been reported by Maturi et al. and Singer et al., who found enhanced and more durable CMT reductions in patients receiving combined therapy compared with anti-VEGF monotherapy [15,16]. Combined therapeutic strategies have demonstrated superior efficacy in rapidly reducing retinal fluid and central retinal thickness, compared to monotherapy, thereby minimizing the duration of edema and the risk of chronic anatomical disruption [17].

This pathophysiological principle has been reiterated by studies showing that persistent intraretinal edema is associated with disruption of the ellipsoid zone, loss of photoreceptors, and retinal thinning, all of which correlate with a poorer functional prognosis [17–20]. In this regard, modern therapeutic strategies seek not only to resolve the existing edema, but also to interrupt the inflammatory and vascular cycle that promotes its chronicity.

In our study, 76.9% of eyes achieved a post-treatment CMT below 300 µm, comparable to the anatomical success rates reported in the GENEVA trial using a Dexamethasone implant [21,23], and superior to real-world outcomes of single-agent Triamcinolone or anti-VEGF treatment. The above may suggest that aggressive control of macular edema with combined therapy is critical to try to prevent the cascade of anatomical changes associated with prolonged retinal fluid accumulation, which can result in irreversible structural damage and permanent visual dysfunction.

In regard to complications, mean IOP remained stable (15.18 mmHg pre- vs. 15.69 mmHg post-intervention), and ocular hypertension occurred in only 17.2% of CRVO eyes – lower than rates reported in SCORE and GENEVA, in which up to 30–35% of patients required IOP-lowering medications [14,21,22]. Cataract progression was observed in 12.82% of our total cohort, consistent with the corticosteroid-induced lens changes described in previous reports [16,23,24].

When analyzed by RVO subtype, all groups demonstrated anatomical improvement, with the most pronounced functional gain observed in the IT-BRVO subgroup, where mean BCVA improved from 0.70 ±0.26 to 0.18 ±0.00 LogMAR. Although this subgroup was small, the results suggest that localized branch occlusions may achieve greater visual recovery compared to diffuse CRVO-related edema. Similar patterns have been highlighted in meta-analyses, indicating that BRVO tends to have more favorable visual outcomes than CRVO under pharmacologic therapy [25].

The combination regimen in our cohort was well tolerated and associated with a relatively low intravitreal reinjection burden (mean 3.2 ±3.2 anti-VEGF reinjection and 1.7 ±1.2 steroid reinjections over 18.7 months). These findings align with studies demonstrating that adjunctive corticosteroids can prolong treatment intervals and reduce

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the number of anti-VEGF intravitreal injections required to maintain retinal anatomy and retinal function [15,26, 27]. The complementary pharmacologic mechanisms – VEGF inhibition and anti-inflammatory action – probably explain the sustained effect and low recurrence rates observed.

The main limitations of this study include its retrospective design, limited sample size, and lack of a control group treated with monotherapy, which limits the ability to infer direct superiority. In addition, the heterogeneity in the anti-VEGF agents (Bevacizumab, Ranibizumab, Aflibercept) and corticosteroids (Triamcinolone, Dexamethasone implant) introduces potential variability in treatment response. Nonetheless, the consistent functional and anatomical improvements across all diagnostic subgroups reinforce the therapeutic benefit of the combined approach.

CONCLUSIONS

Combined intravitreal corticosteroid and anti-VEGF therapy produced significant and sustained improvements in both anatomical and functional outcomes in eyes with macular edema secondary to RVO, with an acceptable safety profile and moderate intravitreal reinjection demand. These findings support dual therapy as a valuable option in these patients. Moreover, the rapid and consistent control of macular edema is crucial to prevent irreversible anatomical damage that may compromise long-term visual function, underscoring the rationale for continued and proactive treatment. Further prospective, randomized controlled trials are warranted to validate these results and to optimize combination regimens for different RVO subtypes.

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