Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v2023i1.303
*Biol. Clin. Sci. Res. J., Volume, **2023**: 303*
Original Research Article

EVALUATING EFFICACY AND SAFETY OF SUPRACHOROIDAL TRIAMCINOLONE ACETONIDE FOR PATIENTS WITH RETINAL VEIN OCCLUSION

CHAUHAN K*, SAIGOL HK, AHMAD NI, ALI F, AKHTAR S, RAUF A

Department of Ophthalmology, Sir Ganga Ram Hospital Lahore, Pakistan
**Correspondence author email address: drkhurramchauhan@gmail.com*

(Received, 09th December 2022, Revised 07th April 2023, Published 06th Jun 2023)

Abstract: *The prospective study was conducted in the Ophthalmology department, Sir Ganga Ram Hospital, Lahore, from January 2022 to January 2023 to compare the efficacy and safety of intravitreal (IVT) Bevacizumab alone with the suprachoroidal injection of CLS-TA (an injectable form of triamcinolone) along with IVT Bevacizumab in patients with retinal vein occlusion (RVO) induced macular edema in treatment naïve patients. Participants were randomized 1:1 to the IVT Bevacizumab group, and suprachoroidal injection of CLS-TA combined with IVT Bevacizumab group. Participants in both groups were administered drugs and monitored for 30 minutes after the injections. The final evaluation was done after 3 months. Results showed that the Bevacizumab group required 22 re-treatments of the participants for 3 months follow-up, while the combination group required 8 re-treatments (P=0.013). Regarding safety, 1 patient had cataract progression unrelated to the study drug. Combining steroids with vascular endothelial growth factor (VEGF) suppression benefits RVO-induced macular edema. It improves vision, reduces injection frequency, and provides rapid resolution. It is also seen that suprachoroidal delivery of CLS-TA is associated with a reduced risk of increased IOP and cataract progression compared to typical intraocular steroids.*

Keywords: Suprachoroidal Triamcinolone Acetonide, Retinal Vein Occlusion, Macular Edema

Introduction

Retinal vein occlusion (RVO) is a major ischemic retinopathy. Central RVO (CRVO) results from thrombosis of a major outflow vessel in the eye, while thrombosis of the proximal branch of the central vein results in branch RVO (BRVO). CRVO compromises the venous return of the entire retina, whereas BRVO compromises a retina segment drained by that vessel. Retinal circulation does not have any collateral flow. As a result, the central retinal vein is the only outlet for the blood entering through the central retinal artery. Thus, obstruction of the whole branch of the central retinal vein leads to CRVO or BRVO, causing retinal ischemia (Altintas and Ilhan, 2022; Poh et al., 2020).

RVO affects vision mainly due to macular edema. A study showed that vascular endothelial growth factor (VEGF), a hypoxia-regulated gene product, is a major cause of macular edema (Spooner et al., 2019). Intravitreal injection of VEGF-neutralizing proteins is the first management line for RVO-associated macular edema. It shows an effective response in most patients; however, in some patients, it has a suboptimal response, probably due to the action of other hypoxia-stimulated factors. Patients who respond well to VEGF suppression require IVT VEGF-neutralizing protein even after four years for controlling edema. Thus there is a need for additional treatment methods. Corticosteroids cause regression of vascular leakage, angiogenesis, and inflammation, so it is considered an appealing alternative method (Belavy et al., 2022). IVT triamcinolone acetonide (TA) injection has proven useful in managing CRVO but has raised intraocular pressure in significant cases and induced cataracts in a few (Zhang et al., 2020). Intraocular dexamethasone implant improves vision and reduces edema in cases with RVO but is also associated with increased IOP and cataracts in many patients.

Due to these adverse effects, intravitreal steroids are second-line therapy in RVO. Suprachoroidal injection of corticosteroids provides an alternative route of delivery that minimizes the risk of adverse effects (Naftali Ben Haim and Moisseiev, 2021). Suprachoroidal fluorescein-labeled dextrans or sodium fluorescein in rabbits has resulted in 10 fold higher vitreous fluorophotometry level in the retina than in the IVT route (Jung et al., 2019). Insoluble drug particles remain in the suprachoroidal space long after injection. Comparison of TA levels in the anterior segment, choroid, or retina at variable intervals after IVT and suprachoroidal injections

[Citation Chauhan, K., Saigol, H.K., Ahmad, N.I., Ali, F., Akhtar, S., Rauf, A. (2023). Evaluating efficacy and safety of suprachoroidal triamcinolone acetonide for patients with retinal vein occlusion. *Biol. Clin. Sci. Res. J.*, **2023***: 303.* doi: https://doi.org/10.54112/bcsrj.v2023i1.303]

showed that levels in the choroid and retina are 10-fold higher after suprachoroidal injections. In the anterior segment, it is 3% the level seen after IVT injection. Thus, suprachoroidal injections minimizes drug level in anterior segment, reducing the risk of increased IOP and cataract. Using microneedle syringes during administration of suprachoroidal injections reduce risks associated with IVT injection. In this study we aim to compare efficacy and safety of IVT Bevacizumab alone with suprachoroidal injection of CLS-TA along with IVT Bevacizumab in patients with RVO induced treatment naïve macular edema.

Methodology

The prospective study was conducted in the Ophthalmology department, Sir Ganga Ram Hospital, Lahore, from January 2022 to January 2023. The study included male and non-pregnant female patients aged ≥18 years who had RVO-induced treatment naïve macular edema best corrected visual acuity (BCVA) letter score in each eye was ≥ 20 letters on ETDRS chart (6/120) but < 70 letters (6/12) and central subfield thickness (CST) ≥310 µm on OCT. Patients with a history of previous retinal surgery, having IOP of more than 21 mm of Hg or already on Anti glaucoma therapy, having significant media opacity that could hinder the evaluation of the retina, other causes of compromised vision due to other ophthalmic disorders, who had previously taken treatment for RVO and those having macular edema secondary to any other cause were excluded from the study. Informed consent of the participants was taken. The ethical board of the hospital approved the study.

All participants underwent complete eye examination, BCVA was recorded, and CST was measured using a Topcon OCT C2000 machine. Participants were randomized 1:1 to the IVT Bevacizumab group, and suprachoroidal injection of CLS-TA combined with IVT Bevacizumab group. Participants in both groups were administered drugs and monitored for 30 minutes after the injections. Re-treatment (at 1, 2, and 3 months) criteria for IVT injection was i) CST ≥310 µm or ii) more than 10 letters decrease in BCVA than preceding visit or iii) more than 50 mm increase in CST than preceding visit. The final evaluation was done after 3 months.

Data were analyzed using SPSS version 23.0. Categorical variables were represented as frequency and percentage. Quantitative variables were represented as mean and standard deviation. Categorical variables between both groups were compared using the chi-square test and quantitative variables through Student's t-test. Quantitative data in both the groups at baseline, 1, 2, and 3 months were compared using ANOVA. P value > 0.05 was considered statistically significant.

Results

A total of 40 subjects, 20 in each group, were included in the study. In both groups, CST was ~730 µm and BCVA~49. The primary efficacy outcome of the study was to examine the number of re-treatment cases in both groups. Results showed that the Bevacizumab group required 22 re-treatments during 3 months follow-up, while the combination group required 8 re-treatments (P=0.013). Re treatments required in each visit in combination vs. the Bevacizumab group were 1 vs. 3(1st month), 2 vs. 10(2nd month), and 5 vs. 9 (3rd month). 15 (75%) patients in the Bevacizumab group and 6 (20%) patients in the combination group required re-treatment (P=0.003). The secondary efficacy outcome was a comparison of visual outcomes between both groups. The mean baseline BCVA score in the Bevacizumab group was 48.8, and in the combination group was 49. Mean improvement at each follow-up visit in Bevacizumab vs. combination group was 11.5 vs. 16.2 (1st month, P=0.20), 11.8 vs. 20.5 (2nd month, P=0.04) and 11.4 vs. 18.8 (3rd month, P=0.09).

In the Bevacizumab group, 4 (20%) patients had BRVO, 15 (75%) had CRVO, while in the combination group, 12 (60%) had BRVO, and 7 (35%) had CRVO. In the Bevacizumab group, 13 of 15 CRVO patients and 2 of 4 BRVO patients required Bevacizumab re-treatment. In the combination group, 3 7 CRVO patients and 3 12 BRVO patients required Bevacizumab re-treatment. In patients with CRVO, the mean baseline BCVA in the Bevacizumab group was 46.4 letters vs. 40.1 letters in the combination group. The mean BCVA in 1st month in the combination group was 61.2 vs. 56.8 in the Bevacizumab group, which remained consistent during 2nd and 3rd months. The mean baseline CST in combination vs. the Bevacizumab group was 875.5µm vs. 777.5µm, which became 604µm vs. 364 µm in 3rd month. In patients with BRVO, the mean baseline BCVA in both groups was well-balanced, while the mean CST in the combination group was slightly worse. There was no significant difference between both groups during various time intervals, except in 2nd month when mean CST worsened substantially, and mean BCVA worsened slightly in the Bevacizumab group.

Ocular events in both groups are summarized in Table I. In the combination group, 1 patient had cataract progression unrelated to the study drug. 2 patients in the combination group had increased IOP, which was managed by topical drops.

[Citation Chauhan, K., Saigol, H.K., Ahmad, N.I., Ali, F., Akhtar, S., Rauf, A. (2023). Evaluating efficacy and safety of suprachoroidal triamcinolone acetonide for patients with retinal vein occlusion. *Biol. Clin. Sci. Res. J.*, **2023***: 303.* doi: https://doi.org/10.54112/bcsrj.v2023i1.303]

Table I Summary of adverse events

	IVT Bevacizumab group n=20 (%)	IVT Bevacizumab + suprachoroidal injection of CLS-TA n=20 (%)
Total adverse events	11	27
Related	0	7 (26)
Not related	11(100)	20 (74)
Eye disorders		
Cataract	0	1 (5)
Anterior chamber inflammation	0	1 (5)
Conjunctival hemorrhage	1 (5)	2 (10)
Conjunctival hyperemia	1 (5)	0
Corneal edema	0	0
Foreign body sensation	0	2 (10)
Eye pain	1 (5)	7 (35)
Lacrimation increased	0	1 (5)
Macular fibrosis	1 (5)	0
Ocular discomfort	3 (15)	4 (20)
Ocular hypertension	0	2 (10)
Optic disc vascular disorder	0	0
Optic nerve disorder	0	0
Punctate keratitis	0	0
Retinal degeneration	0	0
Retinal hemorrhage	0	2 (10)
Blurred vision	2 (10)	0
Reduced visual acuity	2 (10)	1 (5)
Vitreous humor detachment	0	2 (10)
Vitreous humor floaters	0	1(5)

Discussion

Retinal ischemia in RVO causes an increase in the level of VEGF, which promotes macular edema and retinal vascular leakage. VEGF suppression benefits many patients but proves ineffective in a few, suggesting the precipitation of other pro-permeability factors (Campochiaro and Akhlaq, 2021). A study conducted on retinal vein occlusion showed that some patients had better edema resolution with IVT dexamethasone implant compared to IVT VEGF neutralizing protein (Georgalas et al., 2019). Intraocular steroids reduce VEGF levels and have a longer action duration than IVT VEGF-neutralizing proteins. Thus it was hypothesized that a combination of both may have added effectiveness. However, previous studies reported that intra-vitreal steroids lead to increased IOP and cataract progression in susceptible individuals (Nawar, 2022; Tayyab et al., 2020). Thus, the use of combination therapy during the early course of the disease remains disputed.

In the current study, a combination of IVT Bevacizumab and suprachoroidal CLS-TA caused complete edema resolution in most participants and reduced the need for additional injections compared to IVT Bevacizumab alone. This finding was in line with a previous study that reported that combination therapy with VEGF suppression and steroids provides prolonged relief (Ali et al., 2023). Moreover, there was a significant improvement in BCVA and CST at 3 follow-up months, which shows sustained edema reduction in the combination group. In the IVT Bevacizumab group, mean CST did not decrease to the normal range. It was also seen that major edema reduction and BCVA improvement in combination vs. Bevacizumab occurred in patients with CRVO, which is consistent with the finding of a previous study (Jan et al., 2023). However, a reduced need for re-treatment with combination therapy was seen in both BRVO and CRVO. BRVO and CRVO are chronic diseases. Injection-sparing benefits of combination therapy are convenient and result in long-term visual gains (James et al., 2019).

In the current study,7 patients in the combination group had ocular adverse events associated with the study drug (Price et al., 2020). This is relatively lower compared to adverse events typically resulting from steroids. Cataract progression was unrelated to the drug, and IOP was effectively managed with topical drops. However, it is important to analyze the long-term impact on IOP and lens clarity. The limitation of this study is the small sample size and shorter follow-up. A larger, more detailed study is recommended for detailed analysis.

Conclusion

A combination of steroids with VEGF suppression is beneficial for RVO-induced macular edema. It

[Citation Chauhan, K., Saigol, H.K., Ahmad, N.I., Ali, F., Akhtar, S., Rauf, A. (2023). Evaluating efficacy and safety of suprachoroidal triamcinolone acetonide for patients with retinal vein occlusion. *Biol. Clin. Sci. Res. J.*, **2023***: 303*. doi: https://doi.org/10.54112/bcsrj.v2023i1.303]

improves vision, reduces injection frequency, and provides rapid resolution. It is also seen that suprachoroidal delivery of CLS-TA is associated with a reduced risk of increased IOP and cataract progression compared to typical intraocular steroids.

Conflict of interest

The authors declared absence of conflict of interest.

References

Ali, B. M., Azmeh, A. M., and Alhalabi, N. M. (2023). Suprachoroidal triamcinolone acetonide for the treatment of macular edema associated with retinal vein occlusion: a pilot study. *BMC ophthalmology* **23**, 1-13.

Altintas, A. G. K., and Ilhan, C. (2022). Effects of the epiretinal membrane on the outcomes of intravitreal dexamethasone implantation for macular edema secondary to branch retinal vein occlusion. *Arquivos Brasileiros de Oftalmologia* **86**, 13-19.

Belavy, D. L., Tagliaferri, S. D., Buntine, P., Saueressig, T., Samanna, C., McGuckian, T., Miller, C. T., and Owen, P. J. (2022). Reducing low-value imaging for low back pain: systematic review with meta-analysis. *Journal of Orthopaedic & Sports Physical Therapy* **52**, 175-191.

Campochiaro, P. A., and Akhlaq, A. (2021). Sustained suppression of VEGF for treatment of retinal/choroidal vascular diseases. *Progress in retinal and eye research* **83**, 100921.

Georgalas, l., Tservakis, I., Kiskira, E. E., Petrou, P., Papaconstantinou, D., and Kanakis, M. (2019). Efficacy and safety of dexamethasone intravitreal implant in patients with retinal vein occlusion resistant to anti-VEGF therapy: a 12-month prospective study. *Cutaneous and Ocular Toxicology* **38**, 330-337.

James, D. G., Mitkute, D., Porter, G., and Vayalambrone, D. (2019). Visual outcomes following intravitreal ranibizumab for diabetic macular edema in a pro re nata protocol from baseline: a real-world experience. *The Asia-Pacific Journal of Ophthalmology* **8**, 200-205.

Jan, S., Mahsood, Y. J., and Shahnam, T. (2023). Outcomes of Intravitreal Bevacizumab Combined with Suprachoroidal Triamcinolone Acetonide in Central Retinal Vein Occlusion with Macular Edema. *Pakistan Journal of Ophthalmology* **39**.

Jung, J. H., Chae, J. J., and Prausnitz, M. R. (2019). Targeting drug delivery within the suprachoroidal space. *Drug discovery today* **24**, 1654-1659.

Naftali Ben Haim, L., and Moisseiev, E. (2021). Drug delivery via the suprachoroidal space for the treatment of retinal diseases. *Pharmaceutics* **13**, 967.

Nawar, A. E. (2022). Modified microneedle for suprachoroidal injection of triamcinolone acetonide combined with intravitreal injection of ranibizumab in branch retinal vein occlusion patients. *Clinical Ophthalmology*, 1139-1151.

Poh, S., Tham, Y.-C., Chee, M. L., Dai, W., Majithia, S., Soh, Z. D., Fenwick, E. K., Tao, Y., Thakur, S., and Rim, T. H. (2020). Association between macular thickness profiles and visual function in healthy eyes: The Singapore Epidemiology of Eye Diseases (SEED) Study. *Scientific Reports* **10**, 6142.

Price, K. W., Albini, T. A., and Yeh, S. (2020). Suprachoroidal Injection of Triamcinolone—Review of a Novel Treatment for Macular Edema Caused by Noninfectious Uveitis. *US ophthalmic review* **13**, 76.

Spooner, K., Hong, T., Fraser-Bell, S., and Chang, A. A. (2019). Current outcomes of anti-VEGF therapy in the treatment of macular oedema secondary to branch retinal vein occlusions: a meta-analysis. *Ophthalmologica* **242**, 163-177.

Tayyab, H., Ahmed, C. N., and Sadiq, M. A. A. (2020). Efficacy and safety of suprachoroidal triamcinolone acetonide in cases of resistant diabetic macular edema. *Pakistan journal of medical sciences* **36**, 42.

Zhang, Y., Duan, J., Chang, T., Li, X., Wang, M., and Zhang, M. (2020). Comparative efficacy of intravitreal pharmacotherapy for macular edema secondary to retinal vein occlusion: A protocol for the systematic review and network meta-analysis. *Medicine* **99**.

[Citation Chauhan, K., Saigol, H.K., Ahmad, N.I., Ali, F., Akhtar, S., Rauf, A. (2023). Evaluating efficacy and safety of suprachoroidal triamcinolone acetonide for patients with retinal vein occlusion. *Biol. Clin. Sci. Res. J.*, **2023***: 303*. doi: https://doi.org/10.54112/bcsrj.v2023i1.303]