International Journal of Medical Arts

Volume 5, Issue 1, January 2023

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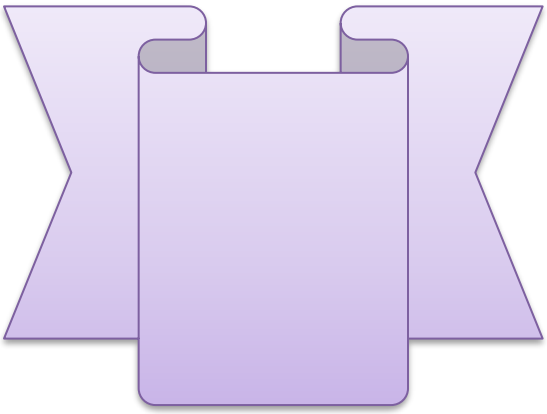

Print ISSN: 2636-4174

Online ISSN: 2682-3780

Available online at Journal Website
https://ijma.journals.ekb.eg/
Main Subject [Ophthalmology]

Original Article

Formulated Posterior Subtenon Triamcinolone Versus Triamcinolone Alone in The Management of Macular Edema Secondary to Non-Ischemic Retinal Vein Occlusions

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Article information

Received: 04-02-2023

Accepted: 07-03-2023

DOI: 10.21608/IJMA.2023.191761.1616

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Citation: Tharwat E. Formulated Posterior Subtenon Triamcinolone Versus Triamcino-lone Alone in The Management of Macular Edema Secondary to Non-Ischemic Retinal Vein Occlusions. IJMA 2023 January; 5 [1]: 2938-2943. doi: 10.21608/IJMA. 2023.191761.1616.

ABSTRACT

Background: Visual impairment, and even blindness, can result from Retinal Vein Occlusion [RVO], making it the second most common vascular disorder of the retina after diabetic retinopathy.

Aim of the Work: To evaluate the effectiveness of the posterior subtenon triamcinolone acetonide [PSTA] alone or formulated in the treatment of macular edema caused by central or branch non-ischemic retinal vein occlusions.

Patients and Methods: Our study included 78 patients, divided into two groups; Formulated PSTA group and PSTA alone group, each of them 39 patients. The NAGATA subtenon cannula was used to administer 40 mg of triamcinolone acetonide [TA] to both groups via the posterior subtenon channel.

Results: At one month, the BCVA improved from 0.4 [0.1 - 0.71] at the baseline to 0.80 [0.10-1.00] in the formulated group, unlike PSTA alone group which was no improvement. This was associated with a reduction in the CMT in the formulated group more than in the PSTA alone group. In the third month, the BCVA increased to 0.90 [0.20-1.00] in formulated group and remain constant in the sixth month. However, in PSTA alone group, the improvement in the BCVA started occurring in the third month which increases from 0.40 [0.10-0.90] at the baseline and the first month to 0.60 [0.20-1.00] in the third month and 0.80 [0.20-1.00] at sixth month. No elevation in the IOP in both groups.

Conclusion: We found that formulated TA is more efficacious than TA alone in improving BCVA and lowering CMT in patients with ME related to Non-Ischemic RVO when administered early in the disease process, without causing any elevation in intraocular pressure.

Keywords: Formulated PSTA; Retinal vein occlusion; Subtenon; Triamcinolone; Macular edema.

INTRODUCTION

Visual impairment, and even blindness, can result from RVO, making it the second most common vascular disorder of the retina after diabetic retinopathy [1]. RVO was classified into central retinal vein occlusion [CRVO], branch retinal vein occlusion [BRVO], and hemi retinal vein occlusion [HRVO] depending on where the occlusion is located [2, 3]. RVO patients have a high risk of developing macular edema. This macular edema may be due to loss of the blood-retinal barrier, caused by damaged tight junctions of the capillary and production of the vascular endothelial growth factors [VEGF] [4].

Treatment options for macular edema include laser photocoagulation [LASER], anti-VEGF, and triamcinolone [1]. Because of its antiangiogenic and anti-inflammatory properties, the corticosteroid triamcinolone acetonide [TA] has been shown to improve visual acuity and decrease central macular thickness in macular edema [5]. Intravitreal triamcinolone acetonide [IVTA] injection is helpful. But it can cause cataracts, high intraocular pressure [IOP], sterile pseudo endophthalmitis, and endophthalmitis [4].

Injecting triamcinolone into the posterior subtenon space is safer than IVTA, However, IVTA is more effective [6]. Our study hypothesizes that increasing the viscosity of triamcinolone by adding sodium hyaluronate and chondroitin sulfate will enhance its scleral time contact and increase its diffusion through the scleral barrier, hence increasing the PSTA's efficacy and decreasing its complications [7].

So, in this study, we aimed to evaluate the efficacy of PSTA injection formulated or alone in the treatment of macular edema post central or branch non-ischemic retinal vein occlusions.

PATIENTS AND METHODS

Our study is a prospective study, which was done from January 2020 to April 2022 in the department of ophthalmology at Al-Azhar University. We included 78 patients complaining of macular edema post-non-ischemic retinal vein occlusions. Patients were randomized into 2 groups PSTA alone group and formulated PSTA group [39 patients for each group]. Our research followed the Helsinki Declaration principles. We got ethical approval from the Damietta Faculty of Medicine [Al-Azhar University]. We recruited the patient after the informed consent as regards the following:

The Inclusion Criteria were 1] visual impairment caused by macular edema as a result of central or branch non-ischemic retinal vein occlusions, 2] CMT of more than 250 µ.

The exclusion criteria were 1] Ischemic RVO, 2] previous laser treatment, 3] ocular diseases such as Glaucoma, cataract, macular ischemia, vitreous hemorrhage, and iris neovascularization, 4] previous injection of anti-VEGFs or steroid three months before the inclusion, 5] Patient with triamcinolone acetonide allergy.

Data collection: Complete medical assessments were done for each patient. General ophthalmologic examinations were done using a slit lamp. Our primary outcomes were the BCVA, IOP, and CMT.

Surgical procedure: Sterilization was done by povidone-iodine [5%]. We anesthetized the conjunctiva with Benoxinate [0.4%], and subconjunctival superior-temporal lidocaine [2%]. Then, we incised the conjunctiva, and tenon seven mm superior-temporal, and posterior to the limbus. Formulated PSTA patients were injected with 40 mg TA, sodium hyaluronate [15 mg] [0.5 ml], and sodium chondroitin sulfate [20 mg]. This formulation was prepared in a 5 ml syringe by good shaking well for 2 minutes. PSTA alone patients were injected only TA by the same TA dose used in the first group. After the injection, the patients were checked on at one, three, and six months.

Statistical analysis: All statistical analysis was done using the SPSS version 25. The normality of the continuous data was tested by the Shapiro–Wilk test. None parametric data were described as medians and ranges. Categorical data were described as numbers and percentages. We compared the qualitative variables by the Chi-square test. Continuous data were compared between study groups using the Mann-Whitney U-test. Within-group comparisons were done using the Friedman test.

RESULTS

Best Corrected Visual Acuity [BCVA]: In the formulated TA group, the BCVA improved at 1–6 months, from 0.4 [0.1 - 0.71] [median

and range] at baseline to 0.8 [0.1 -1] at 1 month and 0.9 [0.2 -1] in the third and 6 months, respectively [p<0.001]. In the TA alone group, the visual acuity did not improve one month after injection, However, it increased from 0.43 [0.1 - 0.75] at the baseline to 0.6 [0.2 -1.01] [p<0.001] and 0.8 [0.2 -1] at the third and sixth months respectively. [Table 2 and Fig. 1]

Reduction in CMT: Table [3] shows a significant reduction in CMT at all follow-up periods in both groups [overall p<0.001]. In the formulated TA group, the thickness reduced from 411 [294 -624] µm at baseline to 208 [178 -531] µm at 6 months [p<0.001], whereas from 412 [293 - 623] µm at the baseline to 215 [187 - 5333] µm at 6 months in the TA alone group [p<0.01]. Also, it shows a significant difference between the two groups at 1, and 3 months [p = 0.001 and =0.040, respectively], while at 6 months there was no significant difference between them [p = 0.204] [Fig. 2].

Intraocular pressure: Table [4] shows a significant decrease from 13 [11 -18] at baseline to 11 [10 -17] after injection in the formulated group [P = 0.014], and from 14 [10 -17] at baseline to 13 [11 -16] after injection in PSTA alone group.

Number of injections: The majority [82.1%] of patients who were treated with the formulated TA did not require a second injection. Re-injection was necessary for a total of 3 patients [7.7%] in the first month, 3 patients [7.7%] in the first and third months, and 1 patient [2.6%] in the third and sixth months [Table 5]. The majority of patients [61.5%] in the TA-alone group got well without additional injections. The re-injection rate was as follows: 23.1% [9 patients] in the first month, 2.6% [only 1 patient] in the third month, 10.3% [4 patients] in both the first and third months, and 2.6% [only 1 patient] in both the third and sixth months [Table 5].

Table [1]: Baseline characteristics

Variable	Formulated TA [n = 39 eyes]	TA [alone] [n = 39 eyes]	P-value [a]
Age, median [range]	59 [50 - 69]	60 [50 - 69]	0.51
BCVA [Decimal]	0.4 [0.1- 0.71]	0.43 [0.1 - 0.75]	1
CMT[µm]	411 [294 - 624]	412 [293 - 623]	0.92
IOP [mmHg]	13 [11-18]	14 [10 -18.5]	1

[a]: Mann-Whitney U-test

Table [2]: Comparison of BCVA over follow-up periods and between the formulated TA group and the TA-alone group

BCVA [Decimal]	Formulated TA [n = 39]	P-value [b]	TA alone [n = 39]	P-value [b]	P-value [c] between groups
Baseline	0.40 [0.1 -0.71]	-	0.43 [0.1 - 0.75]	-	1
1st month	0.8 [0.1-1]	**<0.001****	0.4 [0.1 - 0.91]	**<0.001****	**<0.001***
3rd month	0.9 [0.2 - 1]	**<0.001****	0.6 [0.2 -1.01]	**<0.001****	**0.003***
6th month	0.90 [0.2 - 1]	**<0.001****	0.8 [0.2 -1]	**<0.001****	0.052
P-value [a]	**<0.001***		**<0.001***		

[a]: Friedman Test. [b]: Wilcoxon Signed Ranks Test. [c]: Mann-Whitney U-test. *: statistically significant at P<0.05. **: Statistically significant at P <0.0125 according to post hoc comparison-adjusted by Bonferoni's corrections [p< 0.05/ 4 = 0.0125].

Table [3]: Comparison of CMT over follow-up periods and between the formulated TA group and the TA-alone group

CMT [µm]	Formulated TA [n = 39]	P-value [b]	TA alone [n = 39]	P-value [b]	P-value [c] between groups
Baseline	411 [294 -624]	-	412 [293 - 623]	-	0.980
1st month	264 [187 - 614]	**<0.001****	355 [198 – 616]	**<0.001****	**0.001***
3rd month	222 [187 - 465]	**<0.001****	251 [188 - 467]	**<0.001****	**0.040***
6th month	208 [178 -531]	**<0.001****	215 [187 -533]	**<0.001****	0.204
P-value [a]	**<0.001***		**<0.001***		

[a]: Friedman Test. [b]: Wilcoxon Signed Ranks Test. [c]: Mann-Whitney U-test. *: statistically significant at P<0.05. **: Statistically significant at P <0.0125 according to post hoc comparison-adjusted by Bonferoni's corrections [p< 0.05/ 4 = 0.0125].

Table [4]: Comparison of IOP between the formulated TA group and the TA-alone group at baseline and after treatment

IOP [mmHg]	Formulated TA [n = 39]	P-value [a]	TA alone [n = 39]	P-value [a]	The P-value for between groups
Baseline	13 [11 -18]	**0.041***	14 [10 -17]	**0.041***	1.000
Final	11 [10 -17]		13 [11-16]		1.000

[a]: Wilcoxon Signed Ranks Test. [b]: Mann-Whitney U-test.
*: statistically significant at P<0.05.

Table [5]: Comparison between the formulated TA group and the TA-alone group in resistance and date of re-injection

Resistance and date of re-injection	Formulated TA [n = 39]	TA alone [n = 39]	P-value [a]
No re-injection	32 [82.1%]	24 [61.5%]	
1st-month re-injection	3 [7.7%]	9 [23.1%]	
3rd-month re-injection	0 [0.0%]	1 [2.6%]	0.259
1st and 3rd month re-injection	3 [7.7%]	4 [10.3%]	
3rd and 6th month re-injection	1 [2.6%]	1 [2.6%]	

[a]: Chi-Square [$\chi 2$] test.
*: Statistically significant at P<0.05.

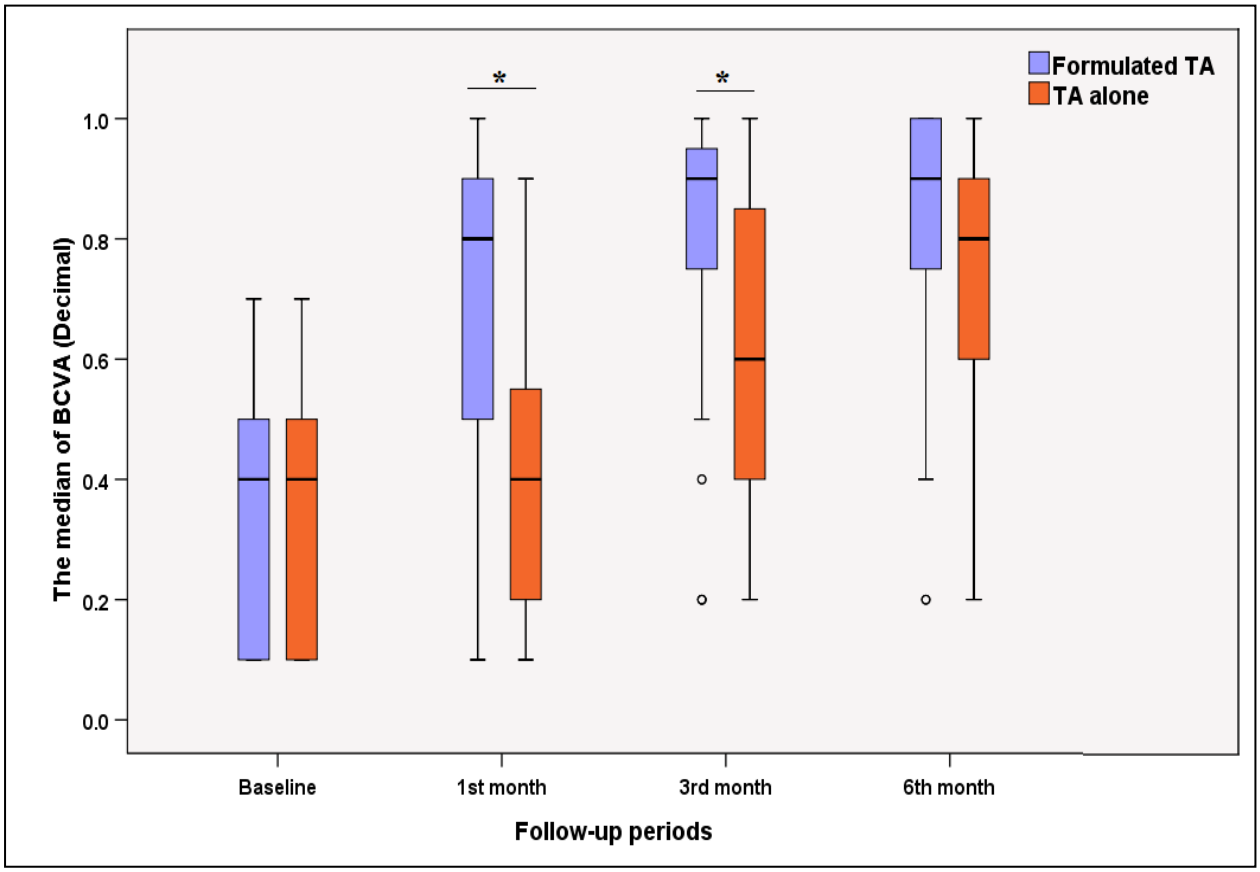

Figure [1]: Box plot representing the BCVA in the study groups. *Statistically significant at P<0.05 [Mann-Whitney U-test]

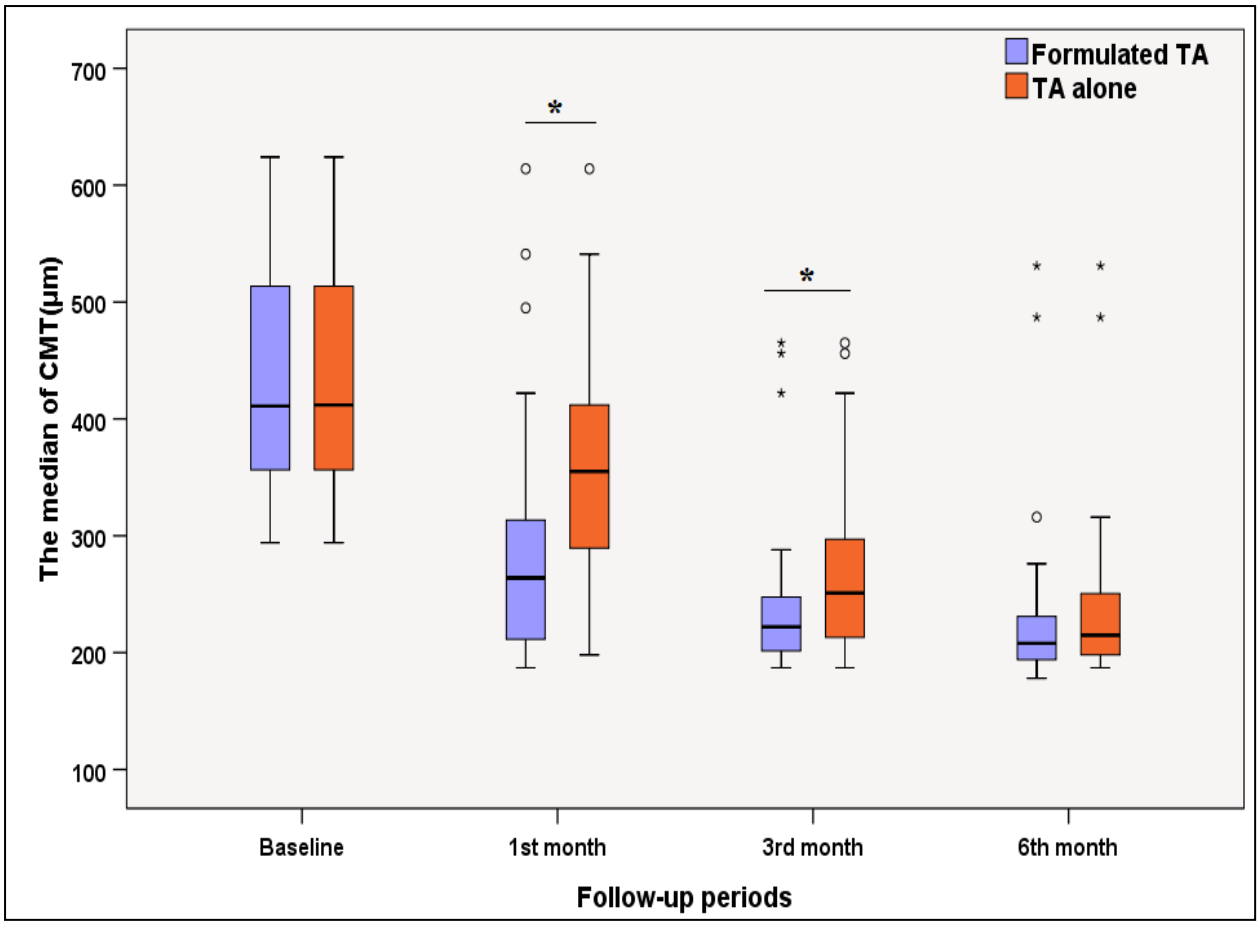

Figure [2]: Box plot representing the CMT in the study groups. *Statistically significant at P<0.05 [Mann-Whitney U-test]

DISCUSSION

Our study showed that the formulated posterior subtenon TA in macular edema patients is superior to TA alone. In the formulated TA group, there was a significant BCVA improvement in all months, however, in the sixth month, neither improvement nor deterioration happened if compared with the third month. In the TA alone group, the improvement in the BCVA was not significant in the first month, the improvement occurred in the third and sixth months but to a degree less than that of the formulated TA group. CMT decreased at all months following therapy in both groups but in Formulated group more than the TA alone. The IOP was not elevated in any group.

TA has anti-inflammatory and antiangiogenic effects that can inhibit VEGF, increasing BCVA and decreasing CMT [5, 8, 9]. The difference between the two groups in the BCVA and CMT is due to the addition of chondroitin sulfate and sodium hyaluronate increasing the viscosity of triamcinolone leading to an increase in the time contact with the sclera [7]. So, the efficacy of TA appeared early and by a higher degree in formulated TA group.

To our knowledge, there is no study comparing the formulated PSTA versus PSTA alone. **Veritti *et al.*** [7] used the formulated TA injection in macular edema secondary to diabetes and found improvement in the visual acuity in 90% of the included subjects, which is in line with our study although different injection sites and populations it strengths our idea that addition of both [sodium hyaluronate, and chondroitin sulfate] increase the efficacy of TA in treating of the macular edema. **Tran *et al.*** [10] looked at 14 eyes for more than three months that had macular edema. They found that PSTA injection is effective in treating macular edema. This is similar to what we found in our study, as we also saw a significant increase in BCVA and a decrease in CMT after PSTA injection. However, they also found an elevation in the IOP by 2 mmHg from the baseline to six months of follow-up in 14% of eyes, which is different from what we found. This may be because they had a smaller sample size.

Another prospective study by **Gurram *et al.*** [11] used the PSTA in the treatment of 24 patients with macular oedema secondary to non-ischemic RVO, resulting in improvement in BCVA and CMT in 79% of patients after one month [p<0.05], which agree with our study results. **Acharya *et al.*** [12] investigated the efficacy of PSTA injection in the treatment of ME due to different retinal conditions, where a BCVA showed significant improvement in 28 eyes [46%] of 60 eyes, which agrees with our results. In 2019, a retrospective study included 1406 eyes of Japanese patients found that IOP elevated by 14.7% after PSTA injection [13], which disagrees with our study, the difference between us may be due to smaller patient age, larger steroid dose, IOP was higher before injection.

Limitations of our study include the small sample size. However, it is the first study in Egypt to compare the Formulated PSTA versus TA alone in patients with macular edema.

In conclusion, formulated TA is more efficacious than TA alone in improving BCVA and lowering CMT in patients with ME related to Non-Ischemic RVO when administered early in the disease process, without causing any elevation in intraocular pressure.

Conflict of interest: none to declare

Funding: none to declare

REFERENCES

1. Costa JV, Moura-Coelho N, Abreu AC, Neves P, Ornelas M, Furtado MJ. Macular edema secondary to retinal vein occlusion in a real-life setting: a multicenter, nationwide, 3-year follow-up study. Graefes Arch Clin Exp Ophthalmol. 2021 Feb;259[2]:343-350. doi: 10.1007/s00417-020-04932-0.

2. Thapa R, Bajimaya S, Paudyal G, Khanal S, Tan S, Thapa SS, van Rens G. Prevalence, pattern and risk factors of retinal vein occlusion in an elderly population in Nepal: the Bhaktapur retina study. BMC Ophthalmol. 2017 Sep 2;17[1]:162. doi: 10.1186/s12886-017-0552-x.

3. Ip M, Hendrick A. Retinal Vein Occlusion Review. Asia Pac J Ophthalmol [Phila]. 2018; 7[1]:40-45. doi: 10.22608/APO.2017442.

4. Kim MW, Moon H, Yang SJ, Joe SG. Effect of Posterior Subtenon Triamcinolone Acetonide Injection on Diabetic Macular Edema Refractory to Intravitreal Bevacizumab Injection. Korean J Ophthalmol. 2016 Feb;30[1]:25-31. doi: 10.3341/kjo.2016.30.1.25.

5. Zhao M, Zhang C, Chen XM, Teng Y, Shi TW, Liu F. Comparison of intravitreal injection of conbercept and triamcinolone acetonide for macular edema secondary to branch retinal vein occlusion. Int J Ophthalmol. 2020 Nov 18;13 [11]:1765-1772. doi: 10.18240/ijo.2020.11.13.

6. Saleh MG, Abdelmoneim MT, Fahmy HL, Riad AN, Lin P. Posterior subtenon versus intravitreal triamcinolone acetonide injection for the treatment of diabetic macular edema. J Curr Med Res Pract 2017;2:141-9. doi: 10.4103/JCMRP.JCMRP_29_16.

7. Veritti D, Lanzetta P, Perissin L, Bandello F. Posterior juxtascleral infusion of modified triamcinolone acetonide formulation for refractory diabetic macular edema: one-year follow-up. Invest Ophthalmol Vis Sci. 2009 May; 50[5]:2391-7. doi: 10.1167/iovs.08-2518.

8. McAllister IL, Vijayasekaran S, Chen SD, Yu DY. Effect of triamcinolone acetonide on vascular endothelial growth factor and occludin levels in branch retinal vein occlusion. Am J Ophthalmol. 2009 May;147[5]:838-46, 846.e1-2. doi: 10.1016/j.ajo.2008.12.006.

9. Becerra EM, Morescalchi F, Gandolfo F, Danzi P, Nascimbeni G, Arcidiacono B, Semeraro F. Clinical evidence of intravitreal triamcinolone acetonide in the management of age-related macular degeneration. Curr Drug Targets. 2011 Feb;12[2]:149-72. doi: 10.2174/1389450117941-82746.

10. Tran HV, Ambresin A, Pournaras J-A, Sabani I, Wolfensberger TJ. Posterior Sub-Tenon Triamcinolone Injection for Chronic Macular Oedema Associated With Non-Ischemic Branch or Central Retinal Vein Occlusion. Ophthalmol - Open J [Internet]. 2016 Nov 29;1[1]:9–14. doi: 10.17140/OOJ-1-103.

11. Gurram MM. Effect of posterior sub-tenon triamcinolone in macular edema due to non-ischemic vein occlusions. J Clin Diagn Res. 2013 Dec;7[12]:2821-4. doi: 10.7860/JCDR/2013/6473.3766.

12. Bakri SJ, Kaiser PK. Posterior subtenon triamcinolone acetonide for refractory diabetic macular edema. Am J Ophthalmol. 2005 Feb; 139[2]:290-4. doi: 10.1016/j.ajo.2004.09.038.

13. Maeda Y, Ishikawa H, Nishikawa H, Shimizu M, Kinoshita T, Ogihara R, *et al*. Intraocular pressure elevation after subtenon triamcinolone acetonide injection; Multicentre retrospective cohort study in Japan. PLoS One. 2019 Dec 5;14[12]:e0226118. doi: 10.1371/journal.pone.0226118.

International Journal of Medical Arts

https://ijma.journals.ekb.eg/
Print ISSN: 2636-4174
Online ISSN: 2682-3780