E-ISSN:2456-6454
P-ISSN:2581-4907
RNI:MPENG/2017/74152
Research Article
Macular edema

Tropical Journal of Ophthalmology and Otolaryngology
2022 Volume 7 Number 1 January February

Publisher
MEDRESEARCH
www.medresearch.in

A Study on Intraocular Pressure Elevation after Intravitreal 4mg Triamcinolone Acetonide Injection in treatment of macular edema

Jayakrishnan G.[1*], Suryavanshi D.[2], Giridhar P.[3]

DOI: https://doi.org/10.17511/jooo.2022.i01.04

[1*] Ganeshkumar Jayakrishnan, Assistant Professor, Department of Ophthalmology, Dhanalakshmi Srinivasan Medical College and Hospital, Siruvachur, Perambalur, TN, India.

[2] Deodatt Suryavanshi, Assistant Professor, Department of Social and Preventive Medicine, Dhanalakshmi Srinivasan Medical College and Hospital, Siruvachur, Perambalur, TN, India.

[3] P.S Giridhar, Professor, Department of Ophthalmology, Dhanalakshmi Srinivasan Medical College and Hospital, Siruvachur, Perambalur, TN, India.

Introduction: Macular edema is one of the leading causes of impaired vision in some retinal vascular disorders. Recent clinical studies suggest that intravitreal injection of triamcinolone acetonide (IVTA) may be a therapeutic option for the treatment of macular edema. In 1995, Penfold et al reported a pilot study of intravitreal injection of 4mg of triamcinolone acetonide (IVTA) to treat exudative age-related macular degeneration with encouraging results. **Materials and Methods:** A prospective, non-comparative study was performed with 87 patients (103 eyes) who received 4mg/0.1mL (40g/L) IVTA injection for macular edema and who were followed up for a minimum of 3 months at the Department of Ophthalmology. Patients using steroidal eye drops or systemic steroids, those previously treated with subconjunctival or subtenon steroid injections and those with a prior history of glaucoma were excluded from the study. **Results:** Of the 103 eyes, the mean age was 56.3±11.4 years. Indication for the IVTA was progressive declining of visual acuity due to macular edema associated with retinal venous occlusive disorders or diabetic retinopathy. IOP increased significantly ($p<0.001$) from 14.95±2.83 mmHg preoperatively to a mean maximum of 19.01±5.92 mmHg postoperatively. **Conclusion:** According to our results, intravitreal injection of 4mg of triamcinolone acetonide can lead to significant IOP elevation in approximately one-third of patients, occurring at a mean of 4 weeks after injection. The findings of our study suggest that the IVTA in a dosage of 4 mg could lead to secondary ocular hypertension.

Keywords: Intraocular pressure, Triamcinolone acetonide, Intravitreal steroid injection, Macular odema

Corresponding Author

Ganeshkumar Jayakrishnan, Assistant Professor, Department of Ophthalmology, Dhanalakshmi Srinivasan Medical College and Hospital, Siruvachur, Perambalur, TN, India.
Email: dr_ganti@yahoo.co.in

How to Cite this Article

Ganeshkumar Jayakrishnan, Deodatt Suryavanshi, P.S Giridhar, A Study on Intraocular Pressure Elevation after Intravitreal 4mg Triamcinolone Acetonide Injection in treatment of macular edema. Trop J Ophthalmol Otolaryngol. 2022;7(1):18-22. Available From https://opthalmology.medresearch.in/index.php/jooo/article/view/234

To Browse

Manuscript Received	Review Round 1	Review Round 2	Review Round 3	Accepted
2022-01-18	2022-01-20	2022-01-27	2022-02-03	2022-02-10

Conflict of Interest	Funding	Ethical Approval	Plagiarism X-checker	Note
Nil	Nil	Yes	16%	

Introduction

Macular edema is one of the leading causes of impaired vision in some retinal vascular disorders. Recent clinical studies suggest that intravitreal injection of triamcinolone acetonide (IVTA) may be a therapeutic option for the treatment of macular edema. In 1995, Penfold et al reported a pilot study of intravitreal injection of 4mg of triamcinolone acetonide (IVTA) to treat exudative age-related macular degeneration with encouraging results [1]. Thereafter, intravitreal injection of triamcinolone acetonide became a popular & effective therapeutic option for many conditions, including ocular inflammatory diseases [2]. retinal venous-occlusive disease, [3]. diabetic macular edema [4]. and ocular choroidal neovascularization [5]. One of the major ocular side effects of corticosteroids is the elevation of intraocular pressure (IOP). [6,7].

Intravitreal steroid injections have been widely used in the field of ophthalmology since intravitreal dexamethasone injection was first used in the treatment of endophthalmitis by Graham and associates in 1974.8 Amongst the steroids, triamcinolone acetonide is hydrophobic and therefore, its concentration levels can persist in the vitreous for up to 3 months [9,10]. In addition, its fibroblast growth inhibitory effect is 21-fold more forceful than that of dexamethasone.

Intravitreal triamcinolone acetonide (IVTA) injection has been widely used to treat several intraocular neovascular, inflammatory, and edematous diseases [11-16]. However, steroid-induced increase in the intraocular pressure (IOP) is one of the most widely cited side effects of IVTA injection.17,18 A significant amount of corticosteroid passes into intravitreal tissues after the injection, leading to a significant elevation in the IOP.

As the spectrum of indications grow wider and thereby the use of IVTA increases, the incidence of corticosteroid-induced glaucoma associated with IVTA will become more commonly encountered by ophthalmologists. The main purpose of this study is to conduct a prospective study & analysis on IOP changes following IVTA-injections and to determine any correlation or risk factors between various age groups & periods. Such an analysis will shed light on the progression of IOP following an IVTA injection and allow for comparing possible advantages and disadvantages of the procedure.

Materials and Method

A prospective, non-comparative study was performed with 87 patients (103 eyes) who received 4mg/0.1mL (40g/L) IVTA injection for macular edema and who were followed up for a minimum of 3 months at the Department of Ophthalmology. Patients using steroidal eye drops or systemic steroids, those previously treated with subconjunctival or subtenon steroid injections, and those with a prior history of glaucoma were excluded from the study. Written informed consent was obtained from each participant of the study. The study was approved by the Institutional Ethics Committee on Human Studies (IECHS) and the Institutional Research Committee (IRC), adhering to the tenets of the Declaration of Helsinki.

The procedure was administered with topical anesthesia. After sterilization of the periocular area with 5% povidone-iodine, 4 mg triamcinolone acetonide was injected with a 26 G needle at the inferonasal or inferotemporal site, 3.5 mm from the limbus. Paracentesis was not performed. Patients were maintained in an upright position for 24 hours after IVTA injection and antibiotic topical medication (gatifloxacin) was instilled, 1 drop 4 times per day for 1 week.

Each patient's IOP was evaluated before the procedure, 14 days after the injection was given, and monthly thereafter, using a noncontact tonometer (TOPCON CT-80). Mean IOP of three measurements was used. Wherever the intraocular pressure values recorded by the noncontact tonometer was over 5 mmHg of the previous measurement or not recordable, the IOP was rechecked with the Goldman applanation tonometer to reduce errors. A significant IOP elevation was defined as an increase of 5 mmHg or more, as recorded on their first examination. Correlations with age, sex, underlying diabetes mellitus or hypertension, refractive error, and previous intraocular surgical history were also analyzed to investigate the factors related to IOP elevation and progression.

Results

Of the 103 eyes, the mean age was 56.3±11.4 years. The reason for the IVTA was the progressive decline of visual acuity due to macular edema associated with diabetic retinopathy (60 eyes) or retinal venous occlusion (43 eyes).

Table 1: Intraocular pressure (mean±SD) before and after the intravitreal injection of 4mg triamcinolone acetonide; P-value: the difference between the postoperative value and the preoperative value.

	Number of eyes	IOP (mmHg)	P
Pre-op	103	14.95±2.83	<0.001
14d post-op	103	15.98±2.57	<0.001
1mo post-op	103	19.01±5.92	<0.001
2mo post-op	103	18.04±5.61	<0.001
3mo post-op	103	17.12±4.31	<0.001
4mo post-op	103	16.73±2.84	<0.001
5mo post-op	103	15.81±2.37	<0.001
6mo post-op	103	15.76±2.10	<0.001

IOP increased significantly ($p<0.001$) from 14.95±2.83 mmHg preoperatively to a mean maximum of 19.01±5.92 mmHg postoperatively.

Table 2: The number of eyes with IOP elevation above baseline in each interval after the intravitreal injection of 4mg triamcinolone acetonide.

	14d	1mo	2mo	3mo	4mo	5mo	6mo
IOP rise ≤5 mmHg	100	72	79	88	99	103	103
IOP rise ≥5 mmHg to 10 mmHg	5	25	18	12	4	0	0
IOP rise ≥10 mmHg	1	16	6	3	0	0	0

A rise in IOP to all values higher than 5mmHg was observed in 6(~5.8%) eyes 14 days after injection. Subsequently, peak values were recorded during 1 month after injection, in a total of 31(30%) eyes, of which 16(15.5%) eyes had an increase in IOP of 10mmHg or greater. At 3 months interval, a reduction in effects of IVTA was noted as 15(14.5%) eyes demonstrated an increase in IOP of 5 mmHg or greater. Within 5 months after IVTA injection, IOP values in all eyes returned to preoperative baseline levels.

Discussion

Macular edema is the major cause of decreased visual acuity in diabetic retinopathy and retinal vein occlusion. A damaged blood-retinal barrier due to capillary leakage can cause macular edema. Corticosteroids have long been known to strengthen blood vessels, hence resulting in a decrease in vessel leakage. Triamcinolone acetonide was demonstrated to reduce the breakdown of the blood-retinal barrier after intravitreal application [19]. and was used to Treat macular edema secondary to retinal vein occlusion [20,21]. and diabetic retinopathy utilizing anti-inflammatory and blood-retinal barrier stabilizing effects [19,22-24]. Corticosteroids are well known for their effectiveness in the inhibition of prostaglandin, [25]. inflammatory adhesion molecules such as ICAM-I and MHC-II, growth factors such as vascular endothelial growth factor (VEGF) and the induction of plasminogen activator inhibitor (PAI)-1. As a result, they strengthen the blood vessels and maintain the integrity of the blood-retinal barrier. Consequently, steroids have been used for the treatment of various ocular diseases, when applied either topically or systemically. However, the eyes account for only 0.01% of the entire body volume, so to treat ocular disease, systemic medication in the place of direct intraocular injection will need a significantly higher dosage to reach the same intraocular concentration, with the potential increased risk of developing systemic side effects.

Jonas17 have also reported the IOP responded to intravitreal injection of 8 mg triamcinolone acetonide. In this retrospective review of 103 eyes of 87 patients, 52% of eyes experienced a pressure elevation higher than 21mmHg with the rise occurring at a mean of 2 months. In our study, the elevation of intraocular pressure was seen at 14 days and peaked at 2 months after IVTA. It is not known whether the responses that were seen in these diabetic subjects were genetically determined or merely modified by ocular complications or other vascular, metabolic, or endocrine changes in diabetes [26].

As described above, IOP elevation after IVTA injection is a common and now well-documented side-effect, but with a large variation in incident rate. Considering some of the patients whose IOP was not controlled and who had to undergo filtering surgery or vitrectomy, determining the risk factors of IOP elevation and the patterns of increased IOP after IVTA injection will provide considerable help in prescribing the treatment, recommending the injection and observing the follow-up. Accordingly, in this study, we investigated the known risk factors of IOP elevation from the usage of systemic or topical steroids. Regarding the difference in the mean elimination half-life of triamcinolone in the vitrectomized eye and the non-vitrectomized patients, we investigated the relations of IOP elevation based on previous intraocular surgical history.

From a clinical point of view, it may be important that in all eyes, the IOP could be controlled by the usage of topical anti-glaucoma medications, meaning that it is feasible to inject triamcinolone acetonide to vitreous.

Conclusion

According to our results, intravitreal injection of 4mg of triamcinolone acetonide can lead to significant IOP elevation in approximately one-third of patients, occurring at a mean of 4 weeks after injection. The findings of our study suggest that the IVTA in a dosage of 4 mg could lead to secondary ocular hypertension; that the rise of IOP may persist at least 5 months after the injection; that the rise of IOP can usually be controlled by topical anti-glaucoma medication; and that the steroid-induced ocular hypertension may thus not be a major contraindication against the use of intravitreal triamcinolone acetonide as treatment trial of macular edema owing to diabetic retinopathy and retinal vein occlusions.

Reference

01. Penfold PL, Gyory JF, Hunyor AB, Billson FA. Exudative macular degeneration and intravitreal triamcinolone. A pilot study. Aust N Z J Ophthalmol. *1995 Nov;23(4):293-8. doi: 10.1111/j.1442-9071.1995.tb00179.x [Crossref][PubMed][Google Scholar]*

02. Young S, Larkin G, Branley M, Lightman S. Safety and efficacy of intravitreal triamcinolone for cystoid macular oedema in uveitis. Clin Exp Ophthalmol. 2001 Feb;29(1):2-6. *doi: 10.1046/j.1442-9071.2001.00360.x [Crossref] [PubMed][Google Scholar]*

03. Greenberg PB, Martidis A, Rogers AH, Duker JS, Reichel E. Intravitreal triamcinolone acetonide for macular oedema due to central retinal vein occlusion. Br J Ophthalmol. 2002 Feb;86(2):247-8. *doi: 10.1136/bjo.86.2.247 [Crossref][PubMed] [Google Scholar]*

04. . . Br J Ophthalmol. 2002 Feb;86(2):247-8. *doi: 10.1136/bjo.86.2.247 [Crossref][PubMed][Google Scholar] [Crossref][PubMed][Google Scholar]*

05. Jonas JB, Söfker A. Intraocular injection of crystalline cortisone as adjunctive treatment of diabetic macular edema. Am J Ophthalmol. 2001 Sep;132(3):425-7. *doi: 10.1016/s0002-9394(01)01010-8 [Crossref][PubMed][Google Scholar]*

06. Danis RP, Ciulla TA, Pratt LM, Anliker W. Intravitreal triamcinolone acetonide in exudative age-related macular degeneration. Retina. 2000;20(3):244-50. *[Crossref][PubMed][Google Scholar]*

07. McLean JM. Use of ACTH and cortisone. Trans Am Ophthalmol Soc1950;48:293–6. *[Crossref] [PubMed][Google Scholar]*

08. Francois J. Cortisone et tension oculaire [Cortisone and eye strain]. Ann Ocul (Paris). 1954 Sep;187(9):805-16. *French [Crossref][PubMed] [Google Scholar]*

09. Graham RO, Peyman GA. Intravitreal injection of dexamethasone. Treatment of experimentally induced endophthalmitis. Arch Ophthalmol. *1974 Aug;92(2):149-54. doi: 10.1001/archopht.1974.01010010155016 [Crossref][PubMed][Google Scholar]*

10. Beer PM, Bakri SJ, Singh RJ, Liu W, Peters GB 3rd, Miller M. Intraocular concentration and pharmacokinetics of triamcinolone acetonide after a single intravitreal injection. Ophthalmology. 2003 Apr;110(4):681-6. *doi: 10.1016/S0161-6420(02)01969-3 [Crossref][PubMed][Google Scholar]*

11. Jonas JB. Intraocular availability of triamcinolone acetonide after intravitreal injection. Am J Ophthalmol. 2004 Mar;137(3):560-2. *doi: 10.1016/j.ajo.2003.08.012 [Crossref][PubMed] [Google Scholar]*

12. Martidis A, Duker JS, Greenberg PB, Rogers AH, Puliafito CA, Reichel E, et al. Intravitreal triamcinolone for refractory diabetic macular edema. Ophthalmology. 2002 May;109(5):920-7. *doi: 10.1016/s0161-6420(02)00975-2 [Crossref] [PubMed][Google Scholar]*

13. Ip MS, Kumar KS. Intravitreous triamcinolone acetonide as treatment for macular edema from central retinal vein occlusion. Arch Ophthalmol. 2002 Sep;120(9):1217-9. *[Crossref][PubMed] [Google Scholar]*

14. Antcliff RJ, Spalton DJ, Stanford MR, Graham EM, ffytche TJ, Marshall J. Intravitreal triamcinolone for uveitic cystoid macular

Edema: an optical coherence tomography study. Ophthalmology. 2001 Apr;108(4):765-72. *doi: 10.1016/s0161-6420(00)00658-8 [Crossref] [PubMed][Google Scholar]*

15. Benhamou N, Massin P, Haouchine B, Audren F, Tadayoni R, Gaudric A. Intravitreal triamcinolone for refractory pseudophakic macular edema. Am J Ophthalmol. 2003 Feb;135(2):246-9. *doi: 10.1016/s0002-9394(02)01938-4 [Crossref] [PubMed][Google Scholar]*

16. Tano Y, Chandler D, Machemer R. Treatment of intraocular proliferation with intravitreal injection of triamcinolone acetonide. Am J Ophthalmol. 1980 Dec;90(6):810-6. *doi: 10.1016/s0002-9394(14)75196-7 [Crossref][PubMed][Google Scholar]*

17. Danis RP, Bingaman DP, Yang Y, Ladd B. Inhibition of preretinal and optic nerve head neovascularization in pigs by intravitreal triamcinolone acetonide. Ophthalmology. 1996 Dec;103(12):2099-104. *doi: 10.1016/s0161-6420(96)30383-7 [Crossref][PubMed][Google Scholar]*

18. Jonas JB, Degenring RF, Kreissig I, Akkoyun I, Kamppeter BA. Intraocular pressure elevation after intravitreal triamcinolone acetonide injection. Ophthalmology. 2005 Apr;112(4):593-8. *doi: 10.1016/j.ophtha.2004.10.042 [Crossref][PubMed] [Google Scholar]*

19. Smithen LM, Ober MD, Maranan L, Spaide RF. Intravitreal triamcinolone acetonide and intraocular pressure. Am J Ophthalmol. 2004 Nov;138(5):740-3. *doi: 10.1016/j.ajo.2004.06.067 [Crossref] [PubMed][Google Scholar]*

20. Wilson CA, Berkowitz BA, Sato Y, Ando N, Handa JT, de Juan E Jr. Treatment with intravitreal steroid reduces blood-retinal barrier breakdown due to retinal photocoagulation. Arch Ophthalmol. 1992 Aug;110(8):1155-9. *doi: 10.1001/archopht.1992.01080200135041 [Crossref][PubMed][Google Scholar]*

21. Zhang, Y. B. , X. L. *Cheng, and J. Dong. Treatment of diabetic macular edema by dual intravitreal injections of triamcinolone. Int J Ophthalmol (Guoji Yanke Zazhi) 5.6 (2005): 1207-1210 [Crossref][PubMed][Google Scholar]*

22. Ozkiris A, Evereklioglu C, Erkiliç K, Tamçelik N, Mirza E. Intravitreal triamcinolone acetonide injection as primary treatment for diabetic macular edema. Eur J Ophthalmol. 2004 Nov-Dec;14(6):543-9. *[Crossref][PubMed][Google Scholar]*

23. Ciulla TA, Walker JD, Fong DS, Criswell MH. Corticosteroids in posterior segment disease: an update on new delivery systems and new indications. Curr Opin Ophthalmol. 2004 Jun;15(3):211-20. *doi: 10.1097/01.icu.0000120711.35941.76 [Crossref] [PubMed][Google Scholar]*

24. Becker B, Bresnick G, Chevrette L, Kolker AE, Oaks MC, Cibis A. Intraocular pressure and its response to topical corticosteroids in diabetes. Arch Ophthalmol. 1966 Oct;76(4):477-83. *doi: 10.1001/archopht.1966.03850010479003 [Crossref][PubMed][Google Scholar]*

25. Hirooka K, Shiraga F, Tanaka S, Baba T, Mandai H. Risk factors for elevated intraocular pressure after trans-tenon retrobulbar injections of triamcinolone. Jpn J Ophthalmol. 2006 May-Jun;50(3):235-8. *doi: 10.1007/s10384-005-0306-9 [Crossref][PubMed][Google Scholar]*

26. Floman N, Zor U. Mechanism of steroid action in ocular inflammation: Inhibition of prostaglandin production. Invest Ophthalmol Vis Sci. 1977 Jan;16(1):69-73. *[Crossref][PubMed][Google Scholar]*

27. Hirooka K, Shiraga F, Tanaka S, Baba T, Mandai H. Risk factors for elevated intraocular pressure after trans-tenon retrobulbar injections of triamcinolone. Jpn J Ophthalmol. 2006 May-Jun;50(3):235-8. *doi: 10.1007/s10384-005-0306-9 [Crossref][PubMed][Google Scholar]*