ORIGINAL RESEARCH PAPER

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# MISADVENTURES OF INTRAVITREAL TRIAMCINOLONE ACETONIDE – A CASE SERIES

**KEY WORDS:** intravitreal triamcinolone , endophthalmitis, diabetic macular edema, vitritis.

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**ABSTRACT**

Periocular and orbital corticosteroid injections are still used as first choice for selective inflammatory conditions. In macular oedema secondary to diabetes (DME), vein occlusions, etc. intravitreal triamcinolone acetonide (IVTA) is an easily available, low cost and safe treatment option. This case series stresses upon the occurrence of unexpected sterile/infective endophthalmitis (SE/IE) following IVTA, its course and treatment. We encountered three eyes with SE/IE post IVTA. Treatment included vitreous tap, intravitreal injections and/or vitrectomy. SE resolved within 3-4 weeks with persistent floaters. One eye with IE was lost. Acute presumed sterile endophthalmitis following IVTA presents early. Visual outcomes are generally good.1

## INTRODUCTION

IVTA is an established treatment in intraretinal edematous diseases such as DME, vein occlusions, and pseudophakic cystoid macular edema. Though it has lost its favor to Anti VEGF's, but is still an easily available, low cost, safe and time tested alternative or adjunct in non-affording population. Complications include increase in intraocular pressure (IOP), cataract , retinal detachment, vitreous hemorrhage and endophthalmitis . Reported sterile endophthalmitis incidence is around 0.10% - 7.3% whereas that of infective endophthalmitis is 0.38%- 1.7%.[6] With these three cases we have tried to outline symptoms, course and treatment for post IVTA endophthalmitis.[2-5]

### Case 1

53-year-old hypertensive male with chief complaints of sudden, painless diminution of vision in right eye (RE) since one week. Best corrected visual acuity (BCVA) was 5/60 in RE with IOP 13 mm of Hg. Ocular examination showed phakic patient with right supro-temporal branch retinal vein occlusion with macular edema. IVTA was injected under all aseptic precautions. Post injection period was uneventful. Patient returned after 24 hours with quiet anterior segment but marked diminution of vision noted around eight hours after injection. BCVA was 2/60. Vitreous showed dense haze with membranes suggestive of dense virtritis. There was no view of the fundus. Prompt vitreous tap taken and intravitreal vancomycin (1 mg/0.10 mL), ceftazidime (2.25mg/0.10 mL) and dexamethasone (0.4 mg/0.10 mL) given. Frequent topical prednisolone acetate, fortified antibiotics and atropine used. There was no further deterioration and no organisms were detected in vitreous samples by gram staining/ KOH, and standard cultures were negative. Over a period of two weeks the haze reduced with increase in vision, which returned to pre-injection state in six weeks. Persistent floaters disappeared by 12 weeks.

### Case 2

47-year-old diabetic female with chief complaints of painless diminution of vision in the left eye (LE) since 2 months. BCVA of 6/60 in LE and IOP 15 mm of Hg was noted. Ocular examination showed phakic patient with LE DME with moderate non proliferative diabetic retinopathy. IVTA was injected under all aseptic precautions. Review after two hours showed quiet anterior and posterior segments. Patient returned after a week with anterior chamber cells 2+, keratic precipitates with marked diminution of vision. BCVA was 1/60. Vitreous again showed dense haze with membranes suggestive of dense vitritis and no view of the fundus. Vitreous tap was negative and intravitreal antibiotics and steroids given. Frequent topical prednisolone acetate, fortified antibiotics and atropine used. Over a period of four weeks, haze reduced with increase in vision, which returned to pre-injection state in 12 weeks.

### Case 3

63 year old diabetic male with decrease of vision in both eyes. BCVA was 1/60 in the RE and perception of light in the LE. Fundus showed RE proliferative diabetic retinopathy with DME and LE Vitreous haemorrhage. IVTA was planned for the RE with laser and vitrectomy for the LE. IVTA was injected under all aseptic precautions. Reviewed after two hours. Anterior and posterior segments were quiet. Patient returned after 48 hours with redness, pain, watering, hypopyon, corneal edema, with exudates over pupillary area. Vitreous tap taken and intravitreal antibiotics and steroids were given. Frequent topical prednisolone acetate, fortified antibiotics and atropine were used. Tap showed presence of gram negative bacilli sensitive to pipracillin and tazobactam. Within 24 hours, the cornea started melting, with increase in exudates. Relevant I/V antibiotics and intravitreal drugs were repeated. Over a period of three days eye became markedly hypotonous with corneal melting and perforation. Eviceration was done.

## DISCUSSION

In literature, the incidence of sterile endophthalmitis post IVTA is reported to be higher as compared to infective. Sterile and infective endophthalmitis have overlapping presentations with very subtle differentiating features but enormously different outcomes. Through this case series we have tried to enumerate the same (Table I, II).

The various hypothesis postulated for sterile endophthalmitis are an inflammatory reaction to preservatives like benzyl alcohol, size and concentration of the particles used in the triamcinolone formulation and endotoxins in formulations. We noted in our series that a change of pharmaceutical company from the standard one to available one led to inflammation. We therefore infer that particle size and concentration and their method of fractionation might be the reason.[5]

Also as compared to other intraocular steroids like

dexamethasone, TA is more lipophilic. Lipophilicity is an important drug property, which impacts on drug uptake and metabolism. It also plays a dominant role in promoting off-target binding or promiscuity, with increased lipophilicity leading to increased likelihood of binding to unwanted cellular targets and may be a reason for more immunogenicity as compared to dexamethasone.[7-8]

With regard to the IE, under the capsule, gram-negative bacteria have an outer membrane that protects them against certain antibiotics, such as penicillin. The disruption of this membrane is two edged sword as it releases toxic substances called endotoxins but also makes the bacteria vulnerable. Endotoxins contribute to severity of symptoms but also makes it more susceptible to antibiotics. This proves the rationale of steroids with antibiotics for gram negative IE as they can penetrate the outer membrane. Use of higher antibiotics in the first go is also recommended due to multidrug resistance.[9-10]

## CONCLUSION

Acute presumed sterile endophthalmitis following IVTA injection presents early in the postoperative period. Visual outcomes are generally good. Differentiating between SE and IE is of utmost importance for the line of treatment and prognosis.

**Table I - Differentiating features between infective and sterile endophthalmitis**

| Characterstic | Infective endophthalitis | Sterile endophthalmitis |
|---|---|---|
| Time of Presentation | Usually 24-48 hours | From within 24 hours to several days |
| Symptoms | Pain, redness, watering, diminution of vision | Pain ±, diminution of vision |
| Visual acuity | May be severely decreased | Mildly to severely decreased |
| Conjunctival congestion | Present | May or may not be present |
| Corneal edema | May be moderate or severe | Generally none or mild |
| Anterior chamber | AC cells 3-4+ | AC cells 1-2+ |
| Hypopyon | Often present | Generally absent |
| Vitreous | Moderate to severe cells with or without membranes | Mild to severe cells with or without membranes |
| Prognosis | Poor | Fairly good |

**Table II - Salient features of prior similar reported cases and comparative data**

| Study & Authors | Number of cases | SE | IE | Intervention required | Prognosis |
|---|---|---|---|---|---|
| 1.Abdullah O , Kuddusi E. Complications of intravitreal injection of triamcinolone acetonide.[3] | 212 | 1 | 1 | Vitrectomy + silicon oil insertion in IE | Poor for IE Good for SE |
| 2. Westfall A.C., Osborn A., Kuhl D., Benz M.S., Mieler W.F., Holz E.R. Acute endophthalmitis incidence: intravitreal triamcinolone.[4] | 1006 | 1 | 0 | Intravitreal antibiotics | Good for SE |
| 3. Moshfeghi, D. M., Kaiser, P. K., Scott, I. U., Sears, J. E., Benz, M., Sinesterra, et al. Acute endophthalmitis following intravitreal triamcinolone acetonide injection[6] | 922 | 1 | 7 | Tap + intravitreal antibiotics, Vitrectomy +intravitreal antibiotics | Poor for IE |
| 4. Present study | 450 | 2 | 1 | Tap + intravitreal antibiotics, Vitrectomy+ Silicon oil insertion | Good for SE Poor for IE |

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