to Evaluate the Effects of Post-Operative Triamcinolone Acetonide in Chronic Postoperative Cystoid Macular Edema

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Abstract:

Background: Postoperative cystoid macular edema is one of the most important causes of suboptimal visual acuity after uncomplicated cataract surgery. Though most of the cases show resolution, but some cases become chronic even despite medical management. Since the data on Indian population is lacking, we have devised this study to evaluate the effects of postoperative triamcinolone acetonide in chronic postoperative macular edema despite being medically managed for minimum of three months.

Methodology: This observational and interventional study was conducted in department of ophthalmology on patients with chronic postoperative cystoid macular edema that developed after uncomplicated phacoemulsification and posterior chamber lens placement surgery for cataract. Postoperative cystoid macular edema was detected on spectral domain Optical Coherence Tomography (OCT) and it persisted for at least three months, despite appropriate medical management.

Results: With the follow-up period ranging from 6-9 months (average 7.43±1.27 months), a reduction in the mean central macular thickness of 32.08% from 529.43±86.92 to 359.57±59.81 μm was obtained at the end of 1 month. The average central macular thickness at 3 months and 6 months were 282.14±42.93 μm and 244.14±35.32 μm respectively, that is, a decrease of 53.89% was obtained in the mean central macular thickness, at the end of 6 months. The baseline number of letters that could be read was 20.71±5.94. The average number of letters that could be read at 1,3 and 6 month were 33.71±8.01, 37.14±6.74 and 40.28±7.06 (the average gain of letters after 6 months was 94.49%) with five out of seven eyes (71.43%) maintaining a visual gain of 15 or more letters from baseline. Decrease in central macular thickness as well as increase in average number of lines read were significant (p<0.05). During follow-up, no patient had IOP exceeding 21mmhg. No injection-related complications were encountered. No repeated injections were needed.

Conclusion: Intravitreal triamcinolone acetonide is a promising therapeutic method for chronic pseudophakic cystoids macular edema cases which do not respond to medical treatment. Further study with a longer follow-up period and larger series is required to assess the treatment’s long term efficacy and safety and the need for retreatment

Keywords: pseudophakic cystoid macular edema, triamcinolone acetonide, intravitreal injection

Date of Submission: 29 -07-2017
Date of acceptance: 12-08-2017

I. Introduction

Cataract surgeries have good visual outcomes. However, cystoid macular edema may lead to suboptimal visual results post-operatively. Therefore, the post-surgical macular edema is one of the most important causes of suboptimal visual acuity that can occur after any intraocular surgery, namely cataract surgery, even in uncomplicated cases. In such cases, it is also called Irvine-Gass Syndrome (IGS) or Pseudophakic Cystoid Macular Edema (PCME) that was first described by Irvine in 1953 and later defined by Gass et al. [1] Cystoid Macular Edema (CME) occurs due to hyperpermeability of the peri-foveal capillaries, resulting in excessive fluid in the retina and polycystic expansion of the extracellular spaces. The pathogenesis of PCME is multifactorial that includes release of inflammatory mediators, vitreous traction and hypotony during surgery. The major contributing factor however remains to be surgically induced anterior segment inflammation that results in the release of endogenous inflammatory mediators, which disrupt the perifoveal...
retinal capillaries resulting in fluid accumulation. Before the advent of extracapsular cataract extraction technique, the rates of PCME were higher with intracapsular cataract extraction. Not only the technique of surgery but selection of the intraocular lens also plays a role in PCME development. Iris-fixated IOLs have the highest reported rate of PCME and in general, anterior chamber intraocular lenses have higher rates than posterior chamber intraocular lenses. The development of PCME is also influenced by pre-existing systemic and ocular conditions such as diabetes mellitus, hypertension, history of central retinal vein occlusion, recent history of uveitis, pre-existing epiretinal membrane or following complicated cataract surgery such as vitreous loss, iris incarceration in the wound, posterior capsule rupture etc. PCME is an important differential diagnosis of painless decrease in vision following uneventful cataract extraction with the onset typically four to 12 weeks after surgery, with peak incidence from four to six weeks postoperatively. Patients may complain of metamorphopsia, central scotoma and reduced contrast sensitivity and refraction may show a hyperopic shift. PCME can be detected clinically that shows loss of the foveal depression, angiographically using Fluorescein Angiography (FA) or with Optical Coherence Tomography (OCT). Fluorescein angiography findings include perifoveal capillary leakage beginning in the early to mid-frames that increase in size and intensity to form a “petaloid” appearance in later frames, with or without late staining of the optic disc. Spectral-domain OCT has emerged as a sensitive tool for detecting and monitoring PCME and shows cystic spaces in the outer nuclear and outer plexiform layers along with macular thickening. At least one in five patients subjected to uncomplicated cataract surgery develop PCME detected by FA. The advent of spectral-domain OCT has further increased the incidence of PCME due to detection of even minor amounts of intraretinal fluid. However, the incidence of clinically significant PCME is much lower, approximately 0.1% to 2.35%. The natural history of PCME is spontaneous resolution of edema with visual improvement in 3 to 12 months in 80 percent of patients. Only a small proportion of patients will suffer chronic visual morbidity. PCME within 2 months of surgery is classified as acute whereas occurring after 2 months is called chronic. Since, inflammatory mediators such as prostaglandins have a fundamental role in the pathophysiology of PCME, topical Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are initiated with or without topical steroids in acute PCME cases. Topical NSAIDs include drugs such as ketorolac, bromfenac, nepafenac, flurbiprofen etc. For chronic PCME, first-line therapy involves topical combined treatment with NSAIDs and corticosteroids. In refractory PCME cases (4 months of treatment), the patients are treated with intravitreal injections of triamcinolone or anti-VEGF like bevacizumab. Sustained-release corticosteroid intravitreous implants can also be used in such cases. Since the data in Indian population is lacking, we have devised this study to evaluate the efficacy of intravitreal triamcinolone acetonide for the treatment of chronic pseudophakic cystoid macular edema resistant to medical treatment.

II. Materials and methods

This observational study was conducted in Department of Ophthalmology, Government Medical College and Rajindra Hospital Patiala in a period of 10 months from August 2016 to May 2017. Seven eyes of seven patients with chronic pseudophakic CME (four female, three male), aged 54–76 years (average 65 years) were included in the study. Informed consent was obtained from each patient. The eligibility criteria for this study included: (1) PCME confirmed using Spectral-domain OCT, after uncomplicated phacoemulsification and posterior chamber intraocular lens implantation; (2) persistence of the PCME despite medical treatment with topical corticosteroids, topical non-steroidal anti-inflammatory drugs and systemic acetazolamide for at least 3 months; (3) no evidence of vitreous incarceration in the cataract wound; (4) no evidence of ocular disorders, such as uveitis, diabetes mellitus, hypertension, central retinal vein occlusion or pre-existing epiretinal membrane, and (5) no evidence of glaucoma or ocular hypertension.

Intravitreal injection of triamcinolone acetonide (Kenacort-A; 40 mg/ml; Abbott Healthcare Private Limited, India) was used in this study to treat macular edema. Patients were then subjected to visual acuity (with ETDRS chart), Optical Coherence Tomography (OCT) to measure central macular thickness and IntraOcular Pressure (IOP) measurement. After preparation with 5% povidone iodine, topical proparacaine hydrochloride was applied to the ocular surface. The injection consisted of 0.1ml (4mg) of a commercially available suspension of triamcinolone acetonide and was performed using a 27-gauge needle on a 1-ml syringe, 4 mm posterior to the limbus. Indirect ophthalmoscopy was used to confirm proper intravitreal localization of the suspension. The response to treatment was monitored functionally by Visual Acuity (VA) assessment and anatomically by OCT central macular thickness at 1, 3 and 6-month intervals after injection. Potential corticosteroid-induced and injection-related complications were also observed. IOP using Goldmann Applanation tonometer was also monitored in every visit.

III. Statistical analysis:

SPSS (Statistical package for Social Sciences) version 21.0 was the software that was used for testing of data and hypotheses. The data was tabulated as mean ± Standard Deviation (SD).
Seven eyes of seven patients with chronic pseudophakic CME with 4 females and 3 males were included in the study after fulfilling the inclusion criteria. The average age of patients is 65.14±7.73 years (Range from 54-76 years). The average duration of PCME detected by OCT was 8±2.45 months (range from 4-10 months). The average period of follow-up was 7.43±1.27 months (range 6-9 months).

Before intravitreal triamcinolone injection, all eyes had been treated with oral and topical non-steroidal anti-inflammatory drugs, topical steroids and oral acetazolamide. Baseline central macular thickness averaged 529.43±86.92 μm. At 1 month follow-up, a reduction in the mean central macular thickness of 32.08% from 529.43±86.92 to 359.57±59.81 μm was obtained. The average central macular thickness at 3 months and 6 months were 282.14±42.93 μm and 244.1±35.32 μm respectively. So the decrease of 53.89% was obtained in mean central macular thickness, at the end of 6 months. The decrease in central macular thickness is significant (p<0.05). At 6 months follow-up, central macular thickness had increased in one eye when compared with the 3-month results, but as the central macular thickness was less than 300 mm, therefore this increase was not accepted as recurrence and no re-injection was performed. The baseline number of letters that could be read was 20.71±5.94. The average number of letters that could be read at 1,3 and 6 months were 33.71±8.01, 37.14±6.74 and 40.28±7.06. So the average gain of letters after 6 months was of 94.49% with five out of seven eyes (71.43%) maintaining a visual gain of 15 or more letters from baseline. The results are significant (<0.05) From the baseline IOP of 14.42±1.72 mmHg, IOPs rose to 17.14±1.57, 18.15±1.34 and 17.43±1.51 mmHg at 1, 3 and 6 months respectively. During follow-up, no patient had IOP exceeding 21mmHg. No injection-related complications were encountered.

The data of the patients collected is tabulated in table number 1.

### Table 1

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<th>VA (3 mo letter)</th>
<th>VA (6 mo letter)</th>
<th>CMT (initial) μm</th>
<th>CMT (1 mo) μm</th>
<th>CMT (3 mo) μm</th>
<th>CMT (6 mo) μm</th>
<th>IOP (initial) mm Hg</th>
<th>IOP (1 mo) mm Hg</th>
<th>IOP (3 mo) mm Hg</th>
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</table>

VA - visual acuity; CMT - central macular thickness; IOP - intraocular pressure; mo – month

### IV. Discussion

Several studies have established the role of corticosteroids in the cases of pseudophakic macular edema. The role of corticosteroids is based on the proposed pathogenesis of PCME. It is believed that leakage of inflammatory substances from anterior chamber during uncomplicated cataract surgery leads to hyperpermeability of peri-foveal capillaries, resulting in fluid accumulation in layers of retina. Since corticosteroids are arachidonic pathway inhibitors, they break the cascade by decreasing the inflammatory insult to retina. 

The aim of our study was to evaluate the efficacy of intravitreal triamcinolone acetonide for the treatment of chronic pseudophakic cystoid macular edema.

The results of our study found that single intravitreal injection of Triamcinolone acetonide have not only decreased the mean central macular thickness by 53.89% at the end of 6 months but has also increased the gain of letters by 94.49% with five out of seven eyes (71.43%) maintaining a visual gain of 15 or more letters from baseline.

The study conducted by Murat Karacorlu et al in 2003 concluded that intravitreal triamcinolone acetonide is a promising therapeutic method for chronic pseudophakic CME resistant to medical treatment. Their study found decrease in central macular thickness as well increase in gain in number of letters read at the end of 6 months, which are consistent with the results of our study. 

A similar study conducted by Mandi D. Conway et al in 2003 again supported the results of our study by concluding the increase in visual acuity of all patients in their study. Their study, however, needed repeated injections unlike our study. 

In our study, the safety and efficacy of intravitreal triamcinolone in eyes with chronic pseudophakic CME resistant to medical treatment were also evaluated because it is related to serious complications such as glaucoma, cataract, endophthalmitis, and pseudoendophthalmitis. It is caused if a 30-G needle is used instead of a 26 G needle because partial jamming of 30-G needle with crystalline steroid results in high velocity injection of drug in vitreous. All these complications are apart from the risks of retinal detachment and vitreous...
hemorrhage that are inherent to any intravitreal injection. Since the patients in our study were already pseudophakic, complications like cataract were not possible. However, IOP was regularly monitored and all cases showed increased in IOP after injection. Since, not even a single eye was noted to have IOP more than 21mmHg, the anti-glaucoma drugs were not administered in our cases. Taking all precautions relating to sterility in minor operation theatre helped preventing Endophthalmitis. No other complication was observed in our study. Since the drug is milky white fluid that eventually gets absorbed in the vitreous, patients were also explained about the increase in floaters after the procedure.  

The current study has some limitations like the relatively small sample size and the lack of a control group. The duration of follow-up was also relatively short, but the studied intervention appears to have a rapid onset of effect. Positive anatomical and visual responses were apparent at the 1-month post-treatment interval and persisted throughout 6 months of follow-up. However, longer follow-up is required for the establishment of retreatment criteria. So it can be concluded that intravitreal triamcinolone acetone is a promising therapeutic method for chronic pseudophakic CME resistant to medical treatment. Preliminary results show prompt resolution of edema with corresponding improved VA. Further study with a longer follow-up period and larger series is warranted to assess the treatment’s long-term efficacy and safety and the need for retreatment.

**Acknowledgements**

We would like to thank the participants for the study as well as staff of Dept. of Ophthalmology, Government Medical College & Rajindra Hospital, Patiala.  

**Conflict of interest:** None  
**Funding:** None

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*David Aggarwal “To Evaluate the Effects of Post-Operative Triamcinolone Acetonide in Chronic Postoperative Cystoid Macular Edema.” IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) , vol. 16, no. 08, 2017, pp. 08–11.*