OBJECTIVES:
Recalcitrant macular disorders are those retinal conditions which, though treated by various medical and surgical modalities, but showed no improvement in symptoms or visual acuity or both. The present study was carried out to evaluate the efficacy of intravitreal triamcinolone acetonide (TA) injection in patients with these recalcitrant macular disorders.

METHODS:
This prospective and interventional study included 40 patients (40 eyes) having recalcitrant macular disorders. Complete ophthalmic examination such as measurement of intraocular pressure (IOP), visual acuity (log minimal angle of resolution [MAR] units), fundus photography with fluorescein angiography were carried out before and after intravitreal injection of TA. The patients received an intravitreal injection of TA (10 mg) for diabetic macular edema (n=14), age-related macular degeneration (n=13), pars plana cystoid macular edema (CME) (n=5), vascular diseases (n=3), central chorioretinopathy (n=3), and idiopathic CME (n=2). The follow-up was done on day 1, day 7, 1 month, 2 months, and 4 months intervals.

RESULTS:
The mean visual acuity at 2 months (1.12±0.45 log MAR units), and 4 months (1.08±0.46 log MAR units) after the injection were significantly better than baseline measurements (1.32±0.3 log MAR units). The mean baseline IOP was 12.5±2.9 mmHg. The IOP significantly increased after the injection at day 1 and day 7; however, the change in IOP at 1 month, 2 months, and 4 months was not statistically significant.

CONCLUSION:
The results indicate that intravitreal injection of TA in patients with recalcitrant macular disorders caused significant improvement of visual acuity in 10 mg dose.

KEYWORDS:
Intravitreal triamcinolone acetonide, Macular edema, Visual acuity, Intraocular pressure.
patients were recorded. A detailed general and ophthalmic examination was carried out in all patients. Eyes were examined for visual acuity by using the early treatment diabetic retinopathy study (ETDRS) chart, and IOP was measured using noncontact tonometer (NCT) NT-3000 Nidek. The number of letters read by the patient in the chart was converted to log minimal angle of resolution (MAR) units.

Slit lamp biomicroscopy, indirect ophthalmoscopy, and fundus chart was made in each case. Fundus photography done using nidek camera and fluorescein angiography was performed in all cases, and photographs were taken in both early and late phases.

For TA injection, each eye was cleaned using povidone-iodine solution and then draped with sterile aseptic precautions in the operation theater. Infero-temporal quadrant and infero-nasal quadrant were selected for injection in the right and left eye, respectively. The lid speculum was placed after instilling 4% xylocaine. 0.25 ml (10 mg) aqueous suspension of TA (D-cort, DWD Pharmaceutical Private Limited, Mumbai, India) was drawn in 1.0 ml syringe fitted with a 26-gauge needle. The drug was injected through marked site only 2-3 mm deep, so that drug suspension remained in the inferior vitreous cavity and does not interfere in visual axis. Then needle was withdrawn slowly while keeping the site of injection pinched with toothed forceps. Immediately after injection all patients were observed for complications such as vitreous hemorrhage, subconjunctival leakage of drug or prolapsed of vitreous through the injection site. In case of any complication, anterior chamber paracentesis was performed. Ciprofloxacin eye drop and analgesic were given following injection. The patients were kept under observation for about 24 hrs after injection. All patients were reexamined at first post-injection day. The anterior segment was examined with slit lamp for any change in IOP (corneal edema and inflammation). Visual acuity was measured and fundus examination done to rule out any immediate complication. After examination, patients were discharged with topical antibiotic and oral analgesics for 3 days. They were advised to come for follow-up at 1 week, 1 month, 2 months, and 4 months. At each follow-up visit, the patients were examined for visual acuity using ETDRS charts and IOP changes using NCT. In addition, anterior segment examination and fundus examination were done using slit lamp and indirect ophthalmoscope, respectively. If any complication or rise in IOP was noticed during the follow-up period, appropriate medical or surgical treatment was provided to patients.

Statistical analysis
Statistical analyses were made using Graph pad prism software. Nonparametric test Wilcoxon Mann–Whitney rank sum test was used to find the association between variables. A p<0.05 was considered statistically significant.

RESULTS
The study included 40 eyes of 40 patients (17 males and 23 females) who received an intravitreal injection of TA as treatment for diffuse macular edema (n=14), age-related macular degeneration (n=13), pars plana cystoid macular edema (n=5), vascular diseases (n=3), central CHR (n=3), and idiopathic CME (n=2). Mean age of the patients was 51.3±15.8 years (range 16-75 years; median, 52.0 years) (Table 1).

The mean best corrected visual acuity (BCVA) was 1.32±0.3 log MAR units prior to treatment. The mean visual acuity at day 1, day 7, and 1 month was 1.33±0.4, 1.23±0.40, and 1.16±0.44 log MAR units, respectively. There was no significant difference in visual acuity at day 1, day 7, and at 1 month when compared with baseline visual acuity. However, difference in mean visual acuity at 2 month (1.12±0.45 log MAR units) and 4 month (1.08±0.46 log MAR unit) follow-up was found to be statistically significant (p=0.04 and p=0.01) when compared with baseline visual acuity (Fig. 1).

Mean pre-injection visual acuity in DME and ARMD patients was 1.31±0.42 and 1.29±0.27 log MAR units, respectively. At 4 month follow-up, the mean visual acuity was 1.10±0.49 and 1.07±0.32 log MAR units, respectively. Mean pre-injection visual acuity in patients of pars plana CME was 1.06±0.25 log MAR units. Visual acuity improvement to 0.86±0.56 log MAR units was noted at 4 months (p<0.05). No change in mean visual acuity at 4 months was noted in cases of vascular disorders when compared with pre-injection mean visual acuity. In central CHR and idiopathic CME cases mean visual acuity improved to 1.40±0.5 logMAR units and 0.77±0.1 log MAR units, respectively from baseline (pre-injection) visual acuity value of 1.52±0.57 log MAR units and 1.0±0.5 log MAR units, respectively (Fig. 2).

Table 1: Patient demographics in the study

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Range</th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>16-75</td>
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<tr>
<td>Gender (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>17 (42.5)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>23 (57.5)</td>
<td></td>
</tr>
<tr>
<td>Number of eyes (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diffuse macular edema</td>
<td>14 (35)</td>
<td></td>
</tr>
<tr>
<td>Age-related macular degeneration</td>
<td>13 (32.5)</td>
<td></td>
</tr>
<tr>
<td>Pars plana CME</td>
<td>5 (12.5)</td>
<td></td>
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<tr>
<td>Vascular diseases</td>
<td>3 (7.5)</td>
<td></td>
</tr>
<tr>
<td>Central CHR</td>
<td>3 (7.5)</td>
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</tr>
<tr>
<td>Idiopathic CME</td>
<td>2 (5)</td>
<td></td>
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</tbody>
</table>

Table Legend:
- CME: Cystoid macular edema
- SD: Standard deviation
- CHR: Chorioretinopathy

Fig. 1: Mean best corrected visual acuity (log minimal angle of resolution value) following intravitreal triamcinolone acetonide injection, Pre-inj: Pre-injection, D1: Post-injection day 1, D7: Post-injection day 7, M2: Post-injection 2 months, M4: Post-injection 4 months

Fig. 2: Mean pre and post injection best corrected visual acuity (log minimal angle of resolution) among different macular disorders following intravitreal triamcinolone acetonide injection, Pre-inj: Pre-injection, Post-inj: Post-injection, DME: Diabetic macular edema, ARMED: Age related macular degeneration, PP with CME: Pars plana CME, Vas. Dis.: Vascular diseases; Cen CHR: Central chorioretinopathy; Idio CME: Idiopathic CME.
Mean IOP prior to the treatment was 12.5±2.9 mmHg (median, 12.4 mmHg). After injection IOP increased significantly from 12.5±2.9 mmHg to 18.59±8.06 mmHg (median 18.6 mmHg) on day 1 (p=0.001) and 16.4±7.2 mmHg (median 15.0 mmHg) on day 7 (p=0.01). During the follow-up at 1 month, 2 months, and 4 months, the mean IOP were 14.75±4.0 mmHg (median 14.3 mmHg), 14.01±3.79 mmHg (median 13.2 mmHg), and 13.64±3.38 mmHg (median 13.0 mmHg), respectively. There were no significant difference in the mean IOP changes before injection or at 1 month, 2 months, and 4 months after injection (Fig. 3). IOP value in one patient to DME on day 1 after injection reached to 60 mmHg who eventually lost to follow-up after developing sterile endophthalmitis at 1-week follow-up.

Out of 40 patients, 29 patients on fundus examination showed macular edema and rest presented with SRNVM. At 2 month post-injection follow-up, macular edema found to be decreased in 48.2% cases, increased in 6.8% cases, and remained unchanged in 44.8% cases. While at 4 months follow-up edema decreased in 20.6% cases, increased in 20.6% cases, and remained unchanged in 58.6% cases, indicating deterioration. Status of SRNVM was also noticed in follow-up at 1 month. Lesion size was found to be decreased in 50% patients, and no change was noticed in 50% patients. While at 4 months follow-up SRNVM size decreased in 22.2% cases, increased in 22.2%, and remained unchanged in 55.6% patients.

The mean pre-injection and post-injection BCVA at 4 months in patients who presented with macular edema were 1.33±0.39 and 1.17±0.48 log MAR units, respectively. Among the SRNVM cases, mean pre- and post-injection (at 4 months) BCVA was 1.00±0.3 and 1.08±0.37 log MAR units, respectively. The improvement in BCVA in macular edema cases was statistically significant (p=0.01). However, no statistical significant improvement in BCVA was found in SRNVM cases.

**DISCUSSION**

Vision loss in recalcitrant macular disorders is primarily occurring as a result of macular edema. There is a breakdown of the blood-retinal barrier due to capillary leakage and abnormal proliferation of intraocular cells. In addition, the release of vascular endothelial growth factor, cytokines, and other inflammatory mediators play an important role in the pathophysiology of macular edema [28,29]. In recent past use of corticosteroids as an anti-inflammatory agent has shown promising results in the treatment of macular diseases [30,31]. Corticosteroids help in maintenance of blood-retinal barrier as well as facilitate reabsorption of exudates. In addition, these agents have been shown to inhibit the release of vascular endothelial growth factor and synthesis of prostaglandins and leukotrienes, thus suppressing early as well as the late manifestation of inflammation [27,29,32-34].

TA is one of the synthetic corticosteroid that has been used in the treatment of many ocular diseases because of its anti-inflammatory, anti-angiogenic, and anti-permeability actions [35-37]. It can be injected in subconjunctival, subtenon, or retrobulbar space. However, with these applications sufficient intracocular concentration is not achieved, thus to achieve desired therapeutic intraocular concentration it is used as intravitreal injection [27,38,39]. Throughout past decade, TA in the form of intravitreal injection in dose of 4 mg or 20-25 mg has been advocated for the management of many inflammatory, neovascular, and macular edematous conditions of the eye [40-42].

The present study prospectively evaluated efficacy and safety of intravitreal TA in the dose of 10 mg in the treatment of recalcitrant macular disorders. The study included 14 eyes with diabetic macular edema, 13 eyes with age-related macular degeneration, 5 eyes with pars plana cystoid macula edema, 3 eyes with central CHR, 2 eyes with idiopathic CME, and 3 eyes with vascular diseases. The results indicate that a 10 mg dose of intravitreal injection of TA has a beneficial effect in improving the visual outcome up to 4 months follow-up without any significant rise in IOP. In patients of diabetic macular edema and ARM change of mean visual acuity of 0.21 (16%) and 0.22 (16.5%), respectively was found at 4 months. Maximum change in visual acuity of 0.22 (22.2%) was seen in patients of idiopathic CME while no change in visual acuity seen in patients with vascular disorders. These results are in agreement with the findings of other previous studies. Choi et al. [43] reported that visual acuity improved by 0.160 (21.8%) at 1 month and 0.196 (26.8%) at 4 months in patients of diabetic macular edema. Similarly, Jonas et al. [44] reported improvement of 0.15 (15.3%) and 0.19 (19.3%) visual acuity at 1 month and 3 months after injection, respectively. In another study, Jonas et al. [45] showed significant improvement in visual acuity after 2-5 months of intravitreal injection of TA in dose of 25 mg. In ARMD patients, intravitreal TA in the dose of 4 and 20-25 mg has been found to significantly improve the vision in various clinical studies [12,15,44]. Previous clinical and experimental studies have reported that intravitreal TA injection is a safe procedure [3,9,20,8] however, elevation in IOP is considered most common complication following intravitreal TA injection [43,45,46]. Intravitreal TA in 10 mg dose caused an initial significant rise of IOP at day 1 follow-up which gradually normalized to pre-injection values at 4 months follow-up. Other injection related complications such as retinal detachment, retinal necrosis, choroidal detachment, and vitreous hemorrhage were not observed in any patient. Our study has certain limitations as it has no control group, and relatively small number of patients was included in the study. However, the current study differs from previous studies in that we used 10 mg TA to investigate the effect in macular disorders instead of 4 mg or 20-25 mg dose of TA. The results of this study suggest that 10 mg of intravitreal TA might have a beneficial effect in the treatment of macular disorders refractory to previous therapies and side effects mainly IOP rise is insignificant.

**REFERENCES**

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