ORIGINAL RESEARCH PAPER

Ophthalomology

A CLINICAL STUDY ON EFFECT OF POSTERIOR SUB TENON TRIAMCINOLONE ACETONIDE AS AN ADJUNCT TO PAN RETINAL PHOTOCOAGULATION FOR THE TREATMENT OF DIABETIC RETINOPATHY

KEY WORDS: Diabetic retinopathy, Central macular thickness, Posterior sub tenon triamcinolone acetonide

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ABSTRACT

Purpose: To evaluate the efficacy of a single posterior sub-Tenon triamcinolone acetonide (PSTA) injection before pan retinal photocoagulation (PRP) in terms of visual acuity, central macular thickness (CMT) and intra ocular pressure (IOP) **Method:** This prospective, interventional study included 75 eyes of 69 patients with severe non proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) with or without clinically significant macular edema (CSME). To see the effect of PSTA injection, 20mg of triamcinolone was given to one eye of all case group under topical anesthesia, 1 week prior to first session of PRP. Control eye of PRP only group received no prior treatment with PSTA. PRP was performed 3 times at 2week intervals in both eyes. Patients were evaluated on day 0 (baseline), at 1 week, 1 month and 3 months after treatment and the main outcome measures were visual acuity, CMT and IOP. **Result:** At 3 months, mean logMAR BCVA compared with baseline showed significant improvement of 0.420 in PSTA ($p<0.05$) and worsening of 0.07 in control group while mean foveal thickness, showed increase of 5.25μ in control and significant ($p<0.05$) reduction of 73.06μ in PSTA group. IOP increase in PSTA group was insignificant. **Conclusion:** Posterior subtenon triamcinolone injection has shown promising results in prevention of PRP induced visual loss in eyes with diabetic retinopathy by reducing macular thickening.

INTRODUCTION

Diabetes mellitus is a growing global epidemic worldwide that is expected to affect 642 million individuals by the year 2040, leading to an associated increased prevalence of diabetic retinopathy.1 Diabetic retinopathy is one of the commonest causes of blindness in developed countries although, the Early Treatment Diabetic Retinopathy Study (ETDRS) elucidated that scatter laser pan retinal photocoagulation (PRP) minimized the risk of profound visual loss in patients with high-risk proliferative diabetic retinopathy.3-4 Although PRP may put a stop to proliferation in affected retinas, it sometimes causes or aggravates macular edema, which is the main cause of acute visual disturbance Central subfield-involved diabetic macular edema that affects the fovea is a common cause of vision loss in diabetic patients. Diabetic macular edema can be present in any severity level of diabetic retinopathy.1,5-6

Over the past 4 decades, until the recent advent of anti-VEGF therapy, the mainstay of treatment for proliferative diabetic retinopathy was thermal laser photocoagulation in a pan retinal pattern to induce regression of neovascularization. PRP is based on the mechanism to destroy ischemic retina, which produces growth factors, such as VEGF, that is responsible for disease progression. PRP also increases oxygen tension in the eye via 2 mechanisms: (1) decreasing oxygen consumption overall as a result of the purposeful retinal destruction, and (2) increasing the diffusion of oxygen from the choroid in the areas of photocoagulation scars.1 Collectively, these changes results in the regression of existing neovascular tissue and prevent progressive neovascularization. Adverse effects of scatter PRP can leads to precipitation of macular edema or worsening of preexisting edema. Several studies suggested that release of inflammatory factors after laser photocoagulation results in an accumulation of leucocytes in posterior pole which is non-photocoagulated, and upregulation of angiogenic growth factors, such as vascular endothelial growth factor, play an important role in the pathogenesis of the edema, although the exact mechanism of macular edema after PRP has not been explained.7-9.

Triamcinolone acetonide is a corticosteroid that has been reported in previous studies,10 to be efficacious when given by intravitreal injection for the treatment of diabetic macular edema. An intravitreal steroid reduces blood– retinal barrier breakdown that is induced by retinal photocoagulation. Triamcinolone acetonide delivered via the posterior sub tenon route has been used to treat macular edema.11 However, there are insufficient studies on the efficacy and safety of periocular injection of triamcinolone acetonide as adjunctive treatment to PRP. This study is aimed to evaluate the effectiveness of posterior sub-Tenon injection of triamcinolone (PSTA) against PRP induced visual loss and macular thickening in patients with severe non-proliferative or proliferative diabetic retinopathy.

AIM AND OBJECTIVE

To evaluate the efficacy of a single posterior Sub tenon triamcinolone acetonide before pan retinal photocoagulation

MATERIAL AND METHODOLOGY

This study was carried out in the Department of Ophthalmology, Shyam Shah Medical College and associated Gandhi Memorial Hospital, Rewa (M.P.). It was a prospective interventional cohort study.

Case Selection:

All diabetic patients attending Ophthalmology outpatient department either directly or through referral and fulfilling the following study criteria were enrolled for the study.

Inclusion Criteria:

1. Patients with T2DM having severe NPDR or PDR with or without CSME
2. Patients with clear ocular media
3. Patients more than 20 years of age
4. Patients with no other ocular disease
5. All patient who are ready for giving consent for study

Exclusion Criteria:

1. Poorly controlled diabetes (HBA1c >10%)
2. Patients with cataract surgery within the past 6 months
3. Patients with previous history of retinal photocoagulation or vitrectomy
4. Presence of vitreous hemorrhage
5. Known case of glaucoma and ocular hypertension
6. Patient with history of periocular or intraocular steroid injection

Data Collection And Method:
After taking a written informed consent, a comprehensive history was taken which included demographic data and ocular history. A detailed history of diabetes was also taken which included duration of disease and treatment taken. Systemic comorbidities were also enquired about and documented. After enrolment, all patients were subjected to a thorough general and systemic evaluation and comprehensive ocular examination was done.

Ocular Examination:
Comprehensive ophthalmic check-up of the patients was done systemically. Visual acuity (BCVA) was measured with Snellen's chart at 6meter distance which was then converted into LogMAR value. IOP was taken through non-contact tonometry. The normal range of IOP was taken from 10 to 20 mm of Hg. Anterior segment examination was performed using ZEISS Slit-lamp bio-microscope. Neovascularization of iris or any other abnormality if present, was noted. Fundus examination was done after full pupillary dilatation with tropicamide 0.8% and phenylephrine 5%, with direct ophthalmoscope, indirect ophthalmoscope and slit lamp bio-microscopy with a +90 D lens and finding were noted. OCT was done using Carl Zeiss Cirrus SD-OCT 500.

Study Treatment:
To see the effect of PSTA injection, 20mg of triamcinolone acetonide in volume of 0.5ml was given in the supero-temporal quadrant of one eye of all case group patients under topical anesthesia, 1 week prior to first session of PRP. Control eye of PRP only group received no prior treatment with PSTA. PRP was performed 3 times at 2week intervals in all study participants.

Outcome Measurements And Follow Up:
Eyes of the patients were evaluated on day 0 (baseline), at 1 week, 1 month and 3 months after treatment and the main outcome measures were best corrected visual acuity, CMT and IOP. We also evaluated the patients for any treatment (PSTA) related complications.

Statistical Analysis:
The collected data was fed in computer in MS excel and the analysis was performed using the SPSS (Statistical Package for the Social Sciences version 20) for statistics. Student t-test and CHI square test were applied to analyses quantitative variables.

RESULT
In this prospective clinical study, A total of 75 eyes of 69 patients of T2DM with severe NPDR and PDR with or without CSME were included. The disease was bilaterally asymmetrical in 63 patients, for whom, the eye with more advanced diabetic retinopathy was taken as the study eye. The remaining 12 eyes of 6 patients had bilaterally nearly symmetrical disease. All the 75 eyes were randomized into cases (PSTA + PRP) and controls (PRP only) by drawing ballots from sealed envelopes. After this simple randomization, there were 35 eyes in the case group and 40 eyes in control group.

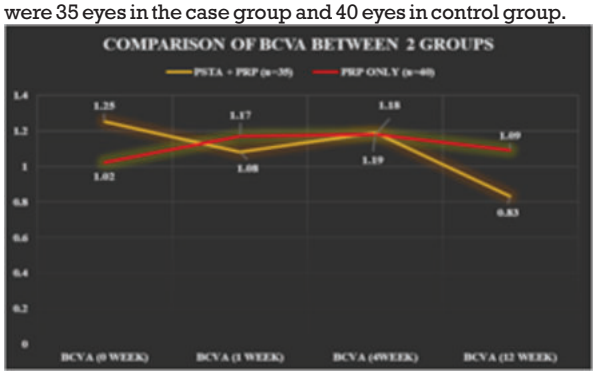


Figure 1

Best Corrected Visual Acuity
In this study, the mean log MAR BCVA increased from baseline to 1st month and dropped again at the end of 3rd months in control group while in case group, the mean logMAR BCVA showed a drop from baseline to 1st week, slight rise from 1st week to 1st month and then showed drop from 1st month to 3rd month.

The mean changes in logMAR BCVA at end of 3rd month compared with BCVA at baseline were improvement of 0.420 in PSTA + PRP group at the same time there was worsening of 0.07 in PRP only group this difference in BCVA was statistically significant($p<0.05$).

Central Macular Thickness
The mean changes in CMT at end of 3rd months compared with CMT at baseline was decrease of 73.06 in PSTA + PRP group at the same time there was increase of 5.25 in CMT in PRP only group and this difference between both the groups was found to be statistically significant ($p < 0.05$).

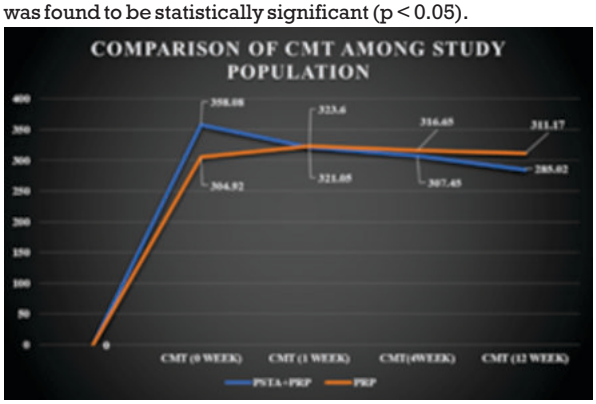
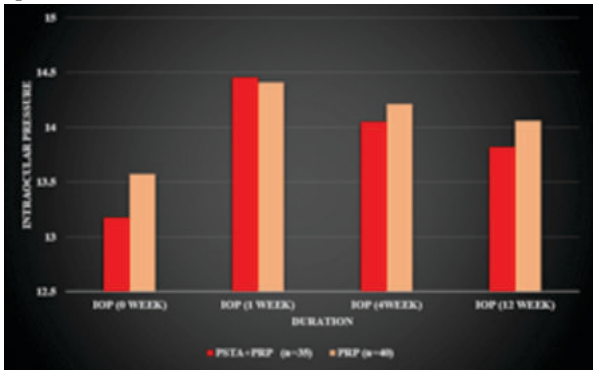


Figure 2

Line graph illustrating clinical course of change in CMT among case group (PSTA + PRP) and control group (PRP only).

Intraocular pressure
Figure 3 compares change in intraocular pressure at 3rd month follow up compared from baseline between case (PSTA + PRP) group and control (PRP only)

group. Change in IOP between primary end point (baseline) and each follow up visits were not statistically significant ($p > 0.05$) within the same group and there was no significant difference seen in IOP between both the groups at each follow up visits



We additionally compared the study outcome parameters in the 6 patients with bilaterally nearly symmetrical disease. The mean logMAR BCVA improved from 1.18 to 0.85 in the case (PSTA + PRP) group whereas the control (PRP only) group showed a worsening of mean visual acuity from 1.08 at baseline to 1.12 at the end of 3-month study period. Similarly, the mean CMT decreased from 325 microns at the initiation of study to 285 in case group while in the control group, it increased from 305 to 335 microns.

When we analyzed the mean values of these three parameters at the final follow-up, we found a statistically significant improvement in both mean logMAR BCVA (p=0.045) and mean CMT (p=0.035) in the cases as compared to controls. The change in mean IOP values between both groups was not significant (p=0.35).

In the present series of 35 patients who received PSTA, no site threatening complications were seen during the study duration. Subconjunctival hemorrhage was seen in 07 patients and 12 patients had complaints about foreign body sensation which got relieved within 2-3 weeks. Rest of the patients did not have any complications.

DISCUSSION

Duration of diabetes is most closely associated with the incidence of diabetic retinopathy and remains the best predictor of diabetic retinopathy. Over the past 4 decades, until the recent advent of anti-VEGF therapy, the mainstay of treatment for proliferative diabetic retinopathy was thermal laser photocoagulation in a pan retinal pattern to induce regression of neovascularization. However, PRP may results in transient reduction in visual function by worsening of macular edema. In previous studies it has been documented that TA reduces macular edema through its stabilizing effect on blood retinal barrier, antiangiogenic and anti-inflammatory action, even though its effect may be transitory. Local administration of drug to the superotemporal quadrant of eye allows maximum absorption of drug through trans scleral route and shows its beneficial effect for up to 12months. To evaluate effect of PSTA prior to PRP in diabetic retinopathy patients, we performed this prospective study in bilateral symmetrical DR patients in order to reduce bias due to systemic factors.

In this study, majority of study participants (60.01%) had poor visual acuity of <6/60 (>1.0 log MAR). The baseline BCVA in PSTA group showed statistically significant (p< 0.001) improvement in BCVA from 1.25 + 0.28 at baseline to 0.83 + 0.23 at the end of 3 months, while in the control group the BCVA showed a worsening from 1.02 + 0.32 at baseline to 1.09 + 0.24 at the end of 3months. The mean changes in log MAR BCVA at end of 3rd month compared with BCVA at baseline were improvement of 0.420 in PSTA + PRP group at the same time there was worsening of 0.07 in PRP only group. Verma LK et al[20] also observed in their study that interventional group patients showed two-line improvement in the visual acuity during follow-up periods while non-intervention had not shown similar improvement in visual acuity and the statistical analysis of their study showed a statistically significant difference in BCVA between both the groups (p= 0.024). Shimura M et al[21] followed their study patients for 6 months and they drew the result from their study that changes in log MAR visual acuity between TA- injected eyes and control eyes was significant at each point of time. Unoki N et al[25] observed similar result in their study and they found that when mean change in log MAR BCVA was compared between both the study groups, there was worsening of 0.010 in PRP only group and an improvement of 0.072 in PRP + PSTA group at the end of 6 months. This observation explains that pre-treatment of diabetic retinopathy patients before PRP added benefits in terms of improvement of BCVA at the end of follow up duration.

In present study, there were no statistically significant differences noted in IOP, either at baseline or at each follow-up point, within the same group, as well as between the two groups. Various other studies by Verma LK et al[20], Unoki N et al[25], Ozkurt YB et al[27] and Yamada Y et al[28] also demonstrated no significant increase in IOP after PSTA injection.

In this study, the mean changes in CMT at end of 3rd month compared with CMT at baseline showed a decrease of 73.06 in PSTA + PRP group, simultaneously there was an increase of 5.25 in CMT in PRP only group. Changes observed during the study duration were statistically significant (p < 0.05). Shimura M et al[21] found in their study that there was a dynamic change seen in central macular thickness after PRP in both PSTA + PRP and PRP only groups. CMT never exceeded 300 microns in PSTA treated eye while it sharply exceeded and reached to 350 microns in control eye. Shima C et al[22] also documented a significant reduction of macular thickness when PSTA was combined with focal laser photocoagulation. Unoki N et al[25] observed in their study that change in mean CMT at 6 months follow up was an increase of 32.8 microns in PRP only group while a decrease of 9.7 microns in PSTA + PRP group, when compared with baseline. Ozkurt YB et al[27] also found similar result in their study which showed beneficial effect of peribulbar steroid injection in CMT when given as an adjunct to PRP in the management of diabetic retinopathy. Yamada Y et al[28] observed that central retinal thickness (CRT) in the pattern scan laser (PSL) group increased gradually at 3 weeks (p=0.01) and then started deceasing. On the contrary, there was a significant reduction in CRT compared with baseline was seen in STTA + PSL group during study duration. These studies favor that PSTA causes significant reduction in central macular thickness when given as an adjunct to PRP for the treatment of DR.

CONCLUSIONS

we conclude that Triamcinolone acetonide given as a posterior sub-Tenon injection can be advantageously and safely used as an adjunct to laser PRP in patients of severe NPDR or PDR, with or without macular oedema.

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