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A Comparative Assessment on Triamcinolone Acetonide Based Alternatives of Laser Photocoagulation Treatments for Diabetic Macular Edema

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ABSTRACT

Macular laser photocoagulation (MLP) a recognized Diabetic macular edema (DME) therapy. Nevertheless, sizeable portion of patients do not react favorably to laser therapy and do not show any improvement after photocoagulation. There are now a growing variety of alternatives to MLP that may be used to treat DME. Comparing the effectiveness of laser photocoagulation with two alternative treatments intravitreal triamcinolone acetonide (IVTA) and a sequential intravitreal triamcinolone acetonide combined with grid laser therapy is the study's goal. The study sincerely attempts to demonstrate the efficacy of existing methods for curing DME by enhancing patient health and simplifying treatment processes. In this study, we have utilized evidence based comparative approach to justify the efficacy of alternative therapies over laser photocoagulation treatment procedure. Facts and resources of experimental cases the data of investigation outcomes of the patient tests are conducted and collected at two hospitals in India. Evidences and experimental results support the efficacy of the alternative treatment method in mitigating adverse effects of laser. Both alternatives, IVTA and triamcinolone acetonide with grid laser are observed effective in enhancing visual acuity, macular thickness and induce reabsorption of hard exudates. Combinational therapy of TA and grid laser is found as a better option than using a grid laser alone in treating diabetes led Macular Edema. The combined therapies have potential to improve visual acuity and decrease central macular thickening.

INTRODUCTION

Problem of Diabetic macular edema (DME) is a kind of retinopathy that is linked to diabetes. This health problem is caused by a condition where fluid accumulates outside the retina because of anomalies in the eye's tiny vessels. In this condition, they carry blood brought on by constant elevations of blood sugar in people with diabetes. Macular edema constitutes around 14% of the total cases of diabetic retinopathies. The severity of macular edema is directly correlated with the duration of diabetes the longer the duration of the disease the more severe the macular edema [1,2].

Currently, the primary methods of treating macular edema involve administering medications like ranibizumab, aflibercept, and triamcinolone acetonide by intravitreal injections, as well as utilizing laser photocoagulation techniques. Macular laser photocoagulation (MLP) is a crucial therapeutic process for DME [3]. It works by increasing the oxidation of the inner retina through thermal effect, which inhibits the production of VEGF. The research conducted by the Early Treatment Diabetic Retinopathy Study Research Group (ETDRS) shown that focal/grid laser treatment has the ability to maintain visual acuity at a stable level[4,5].

Additionally, MLP can shrink retinal blood vessels, decrease intravascular pressure and permeability, and enhance retinal barrier function. These effects help reduce macular edema and improve vision. Reducing macular edema and improving visual acuity are possible outcomes of injecting triamcinolone acetonide (IVTA)[6], which inhibits the proliferation of inflammatory blood vessels and regulates the growth conditions of vascular endothelial. This treatment does not lead to an increase in the occurrence of elevated intraocular pressure or lens opacity when compared to MLP[7]. Indeed, a significant cohort of patients exhibit a lack of response to laser treatment and do not experience improvement following photocoagulation. According to reports, after three years of receiving grid therapy, the visual acuity of 14.5% of eyes improved, remained the same in 60.9% of eyes, and declined in 24.6% of individuals with DMEs. Consequently, IVTA has undergone testing as a potential treatment, whether the condition is new or persistent and unresponsive to laser therapy[8].

These days, there is a proliferation of choices for therapy for DME. Positive results of vascular endothelial growth factor (anti-VEGF)[9] administered intravenously, intravitreal aided release dexamethasone implant, intravitreal and sub-Tenon triamcinolone acetonide (STTA)[10] by injecting and combinational therapies for DME are reported[9]. The most effective treatment for this complex illness is a combination of several approaches[8] that target its many pathways. The blended medicines have the potential to benefit patients and doctors alike by enhancing performance through cumulative effects while minimizing therapy duration and by extension, costs[11].

In this study, the efficacy of two different alternative treatments, (a) Intravitreal triamcinolone acetonide (IVTA) and (a) Sequenced Intravitreal Triamcinolone Acetonide combined with Grid Laser over laser photocoagulation therapy alone. In this research, an honest attempt is made to highlight the improvement in health conditions of patients and reduction in complicacy of treatment processes as can be implemented to cure DME in current time, considering the patient cases in India[12]. The research is an honest endeavor to assess the feasibility and potency of the clinical examination done on triamcinolone acetonide (TA) based DME treatment approaches considering it as better that single laser photocoagulation treatment.

MATERIALS AND METHODS

The study is done as a comparative assessment on alternative approaches that are being utilized currently, such as, (a) intravitreal triamcinolone acetonide (IVTA) and (b) Combinational therapy of Sequential Intravitreal Triamcinolone Acetonide included with Laser Grid to reduce the side effects of laser photocoagulation treatment for DME. Data of the patient test procedures on these two alternatives are collected from the tertiary care hospital. These records are utilized to make the assessment of the efficacies of (a) intravitreal triamcinolone acetonide (IVTA) and (b) Sequential Intravitreal Triamcinolone Acetonide and Grid Laser combined therapy respectively. Patient selection and pre-operative examination for IVTA treatment are given below Inclusion-Exclusion criteria to assess the efficacy of IVTA are:

Inclusion criteria:

- There is no indication of widespread leaking of fluorescein around the macular region
- The central macular thickness (CMT) at baseline is more than 250 µm
- Optimal status of blood glucose
- Blood pressure Compliances
- The subject meeting the mandatory condition of no history of glaucoma (done to assess the increase in intraocular pressure caused by corticosteroids)

Exclusion criteria:

- MDE caused by other health problems
- Advanced state of cataract
- A concise overview of the PRP's history over a span of four months

- Historical background of significant eye surgical procedures. The intraocular pressure is greater than 25 millimeters of mercury

The selected subjects are monitored on their physical conditions, in accordance with the study's aims and objectives. All patients had a comprehensive clinical assessment, which encompassed historical data on the length of the present therapy for systemic disorders such as diabetes mellitus and hypertension. Comprehensive assessments of pulse rate, respiration rate, blood pressure, pallor, icterus and other relevant factors. A comprehensive assessment of the cardiovascular, central nervous, respiratory, gastrointestinal, and excretory systems are done. Examinations performed on the eligible patients are:

- Slit lamp test done to examine anterior portion
- Visual acuity done by Snellen's chart. Conditions selected are distance of 6 meters, counting by fingers, rays guided tests and pinhole detections, BCVA
- Near vision at 20-30 cm range
- IOP check-up
- 90D Fundus test to clinically measure macular swelling level and indirect ophthalmoscopy process
- OCT macula test to examine retina thickness
- FFA to examine focal leakage in the macula region and fundus. Also, to locate ischemic differences observed in fundus (if any)
- Test of Macular function by using Amslers grid at 20-30 cms

Regular screenings, such as Hemoglobin (Hb), Complete Blood Count (CBC), Fasting Blood Sugar, Bleeding Time (BT), Clotting Time (CT), Postprandial Blood Sugar (PPBS) and Kidney Function Tests (KFT) are conducted. Each selected subjects are given a 4 mg, that is, 0.1 mL dose of intravitreal TA while in anesthesia kept under subconjunctival state. In this process, a 26-gauge needle is injected attached to a tuberculin syringe, positioned approx. from 3.5 to 4 millimeter at the position apart from the location of limbus near the temporal parts of pars plana. Patient selection and pre-operative examination for Sequenced Intravitreal Triamcinolone Acetonide combined with Grid Laser are given below Inclusion-Exclusion criteria to assess the efficacy of Sequential Intravitreal Triamcinolone Acetonide combined with Grid Laser process are:

Inclusion criteria:

- Patients of 18 years or older age range detected with Diabetes Mellitus of types 1 and 2 both, according to the standard ADA criteria
- Patients are eligible if they have DME that has affected the fovea, as medically relevant macular edema is an indicator of screening
- Central foveal thickening of 250 microns or higher level, as determined by process of optical coherence tomography

Exclusion criteria:

- Macular edema in individuals without diabetes. Coexistence of proliferative type diabetic retinopathy
- Vitreo macular traction symptoms
- Previous occurrence of glaucoma/elevated eye pressure
- Recent ocular surgery within the past 6 months. There are notable obstructions in the media

During a span of 18.5 months, an unplanned number of 62 eyes from 57 individuals who satisfied our standards for inclusion is collected. Every patient underwent a thorough ophthalmic examination, which comprised various inspections: intraocular pressure (IOP), best-corrected visual acuity (BCVA), fundus fluorescein angiography when required and a baseline measurement of the macular cube using Optical Coherence Tomography. As per the standard treatment protocol, a month later after triamcinolone acetonide therapy by using an intravitreal injection, recipients are treated either with grid laser procedures or grid treatment with laser.

Fig. 1, consisting of 31 eyes from 28 recipients, successfully underwent grid laser procedures as per the established factors. Furthermore, one month after obtaining an intravitreal injection of triamcinolone acetonide, 31 eye samples from 28 selected subjects are deemed suitable for grid based laser stimulation and subsequently completed the medical procedure (Fig. 2). Subsequent assessments were conducted after examination on Day 1, duration of 1 week, 4 weeks, and time of 12 weeks, consisting of comprehensive ocular examination and Optical Coherence Tomography follow-up at each visit. Once, the inclusion and exclusion rules are satisfied and formal informed permission is obtained in writing, the research population underwent a sequence of examinations. Comprehensive historical account Visual acuity assessment using:

- Snellen's chart and refraction
- Ability to perceive colors as assessed using Ishihara's chart
- Inspection of the external part of the eye using a light source and a torch
- Thorough inspection of the eye using a specialized microscope, including measuring the pressure inside the eye using a Goldmann Applanation tonometer

RESULTS

Patient response IVTA treatment are given below: The study included 12 males (92.40%) and 1 female (7.60%). The table given below shows the prevalence of macular edema across different age groups. Correlation between the occurrence of macular edema caused from diabetes of type 2 class and the time length they have had the condition is given in the table below: Enhancement of patient's condition after they are treated with intravitreal injection of triamcinolone acetonide is given in the (Table 1).

Best-corrected visual acuity (BCVA) of patients before and after treatment is given in the Table 4 Best-corrected visual acuity (BCVA) of patients in IVTA treatment Central macular thickness (CMT) tested using optical coherence tomography (OCT) before and after treatment is given in the Patient response Sequential Intravitreal Triamcinolone Acetonide combined with Grid Laser therapy are given below. The mean value of patient's age in Fig. 1 ranges 57.00±7.00 counted in years, whereas in Fig 2, 55.74±7.48 counted in years is the determined range. The age distribution between the two groups do not show any notable disparity as shown in the graph. There was a notable disparity in the distribution of sexes between

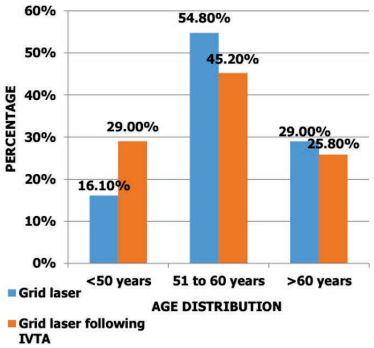

Fig. 1: Age distribution of the two patient groups in Sequential Intravitreal Triamcinolone Acetonide combined with Grid Laser treatment

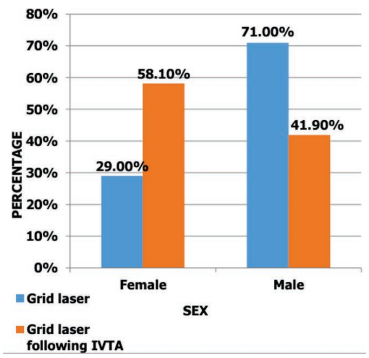

Fig. 2: Sex distribution of the two patient groups in Sequential Intravitreal Triamcinolone Acetonide combined with Grid Laser treatment

Table 1: Prevalence of macular edema across different age groups

Age group	No. of patients (n = 13)	Percentage
51-60 years	09	69.30
61-70 years	03	23.10
71-80 years	01	07.60

Table 2: Individuals having DME caused from type 2 diabetes and patient's responses to IVTA treatment

Group	No. of patients (n = 13) per-treatment	No. of patients (n = 13) per-treatment
Group 1	-	03
Group 2	-	04
Group 3	06	04
Group 4	07	02

Table 3: Patient condition after treated with intravitreal triamcinolone acetonide injection in IVTA process

Group	No. of patients (n = 13) per-treatment	No. of patients (n = 13) per-treatment
Group 1		
Group 2	-	03
Group 3	-	04
Group 4	06	04
	07	02

Table 4: Best-corrected visual acuity (BCVA) of patients in IVTA treatment

visual acuity	BCVA pre intravitreal treatment	BCVA post intravitreal treatment
Log MAR units (mean±SD)	1.2+0.42	0.63+0.33
median	1.0	0.50
Decimal System (mean±SD)	0.09+0.06	0.29+0.17
median	0.10	0.32

Table 5: Central macular thickness (CMT) of patients in IVTA treatment

At baseline mean (±SD)	At 8 months Mean (±SD)	p-value
503.45µm (+210.66µm)	320.76µm (+160µm)	<0.01

the two groups as shown in the Fig 2. Best-corrected visual acuity (BCVA) of patients of two group results are given in the (Table 1-7). Central macular thickness (CMT) measured of patients of two group results are given in the (Table 7).

DISCUSSIONS

IVTA treatment assessment as shown above is summarized below The subjects are selected in this case series had substantial enhancement in visual functioning and pathological appearance of the fundus when tallied to the baseline values and fundus images obtained using fluorescein fundus angiography. This improvement was observed after administering a 4 mg, that is, 1 mL dosage of TA. The conditions that contribute to heightened visual functioning following intravitreal triamcinolone include, Extent of macular ischemia, Enhanced initial visual acuity, Increased intraocular stress seen with subsequent examinations This can be attributed to the pathophysiology of retinal capillaries leaking as a result of diabetes. An elevation of intraocular pressure, or steroid-induced ocular hypertension, was the most noticeable side effect in our research. On the other hand, topical antiglaucoma medications may effectively treat the problem, and optic nerve head cupped is not always necessary.

A mathematical investigation suggests that the presence of triamcinolone grains at the vitreoretinal interface might lead to detached retinal cells or

Table 6: Best-corrected visual acuity (BCVA) of patients in sequential intravitreal triamcinolone acetonide combined with grid laser treatment

	Group								
	Group 1			Group 2			Total		
BCVA Logmar	Mean	SD	p-value in Group 1	Mean	SD	p-value in Group 2	Mean	SD	p-value Between two groups
Baseline	0.665	0.215		0.681	0.178		0.673	0.196	0.749
Day 1	0.671	0.222	0.325	0.477	0.159	<0.001*	0.574	0.215	<0.001*
1 Week	0.658	0.214	0.572	0.477	0.159	<0.001*	0.568	0.208	<0.001*
4 Weeks	0.484	0.250	<0.001*	0.413	0.138	<0.001*	0.448	0.204	0.172
12 Weeks	0.548	0.235	<0.001*	0.523	0.180	<0.001*	0.535	0.208	0.629

Between the group - Independent t test, @ Within the group - Paired t test

Table 7: Central macular thickness (CMT) of patients in Sequential Intravitreal Triamcinolone Acetonide combined with Grid Laser treatment

	Group								
	Group 1			Group 2			Total		
BCVA Logmar	Mean	SD	p-value in group 1	Mean	SD	p-value in group 2	Mean	SD	p-value between two groups
Baseline	411.323	61.952		447.000	73.134		429.161	69.581	0.043*
Day 1	405.387	62.488	<0.001*	267.355	48.827	<0.001*	336.371	89.074	<0.001*
1 Week	379.258	63.576	<0.001*	259.742	46.530	<0.001*	319.500	81.744	<0.001*
4 Weeks	279.000	64.552	<0.001*	247.065	41.336	<0.001*	263.032	56.114	0.024*
12 Weeks	296.581	58.768	0.001*	283.839	48.403	<0.001*	290.210	53.777	0.355

Group 2 patients received grid laser after 1 month of IVTA. # between the groups - Independent t test, @ Within the group - Paired t test

posterior vitreous dissociation. Retinal or posterior vitreous separation was not present in any of the individuals included in the case series that were discussed. Because it has been found to decrease macular edema and vitreoretinal proliferation, posterior vitreous detachment can be beneficial for individuals with diabetic maculopathy and proliferative vitreoretinopathy. The mentioned research did not identify any cases of local side effects such as, sterile endophthalmitis, infectious endophthalmitis, or pseudo endophthalmitis.

The IVTA treatment analysis of the discussed interventional case series aligns together with prior case reports and clinical investigation conducted by [13], suggests that intravitreal triamcinolone may be a viable therapy option for individuals with stubborn macular edema caused by diabetes that does not improve with traditional medical and laser treatments. The IVTA treatment process as discussed here has some limitations. Firstly, the number of patients is limited and do not have control cases for comparison in evaluating the result. Furthermore, there is a dearth of data and research indicating the appropriate dosage that should be administered to patients.

Sequenced Intravitreal Triamcinolone Acetonide combined with Grid Laser treatment assessment as shown above is summarized. Sequential Intravitreal Triamcinolone Acetonide combined with Grid Laser treatment study found no significant difference when determined statistically in the two group's baseline mean best-corrected visual acuity.

At the end of the first one-week, and four-week assessments, Fig. 2 had much better mean best corrected visual acuity than Fig. 1, indicating a significant differences found statistically between the two groups. The most common best-corrected visual acuity of Fig. 1 showed a substantial improvement at both the 4-week and 12-week marks[14].

From the first day to the twelve weeks, Fig. 2 showed a notable increase in their mean best-corrected visual acuity. At baseline, the researchers found no statistically significant difference in the two group's mean central macular thickness. Mean central macular thickening was higher in Group 1 matched with Group 2 1st day, time of 1 week and 4 weeks time. The average central macular thickness in Group 1 decreased significantly from baseline to the following time points: 1 day, 1 week, 4 weeks, and 12 weeks. On days 1-4 and 12 after starting the treatment the mean central macular thickness in Fig. 2 significantly decreased relative to baseline.

At every follow-up, Fig. 2 had a significantly thinner central macular layer than Fig. 1. The research indicates that treating diabetic macular edema with a combination of intravitreal triamcinolone acetonide injections followed by macular grid lasers is more effective. This finding is in line with a study conducted by[8,15], which found that improving visual acuity and decreasing macular edema by 14 weeks was associated with adding 1 intravitreal triamcinolone injection to eyes receiving focal/grid lasers for diabetic macular oedema and panretinal photocoagulation. Nonetheless, the researchers were unable to draw any conclusions on the efficacy of long-term intravitreal therapy, though.

CONCLUSIONS

In this study, we presented two alternative treatments of single practice of laser photocoagulation, namely, (a) intravitreal triamcinolone acetonide (IVTA) and (b) Combination of Sequential Intravitreal Triamcinolone Acetonide and Grid Laser. The experimental findings confirm the effectiveness of the alternative treatment procedure in

terms of reducing the side effects of laser photocoagulation treatment process done on DME patients. The experimental outcome of (a) confirms that visual acuity, macular thickness, and the induction of reabsorption of hard exudates can all be improved by IVTA. If IVTA is to be considered safe for the treatment of DME, further research is required.

The results of outcome of case (b) suggest that laser photocoagulation and intravitreal injection of triamcinolone acetonide can work together to treat diabetic macular edema more effectively than grid laser alone. This combination has the potential to improve visual acuity and reduce central macular thickness.

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