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Intravitreal vs. Subtenon Triamcinolone Acetonide Injection as Adjunctive for Retinal Photocoagulation in Diabetic Macular Edema

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ABSTRACT

Background: Diabetic macular edema (DME) is the predominant ocular consequence of DM and poses a significant risk to patients' vision.

Objective: This study aimed to evaluate the effectiveness of posterior subtenon injection of triamcinolone acetonide (PSTA) compared to intravitreal triamcinolone acetonide (IVTA) prior to argon laser photocoagulation on the best corrected visual acuity (BCVA) in DME.

Patients and methods: This study included 60 eyes with clinically significant macular edema divided into 3 groups of 20 eyes each. Group I received IVTA treatment followed by laser photocoagulation, whereas group II underwent PSTA treatment followed by laser photocoagulation. Group III received treatment solely by laser photocoagulation.

Results: In this study we found that IVTA as an adjunct to laser improved the CMT in 80 % of patients, while PSTA as an adjunct to laser improved the central macular thickness (CMT) in 85 % of patients and laser alone improved only 55% of patients. The percentage of patients who showed an improvement in BCVA at the end of the follow up period was 85 % in the IVTA group and 80 % in the PSTA group and laser alone improved only 55% of patients. IVTA caused a higher rise in IOP and cataract than PSTA, and the IVTA group the risk of complication was higher with IVTA such as disastrous ones such as endopthamitis and retinal detachment.

Conclusion: PSTA injection was comparable to IVTA injection as an adjunctive treatment to argon laser photocoagulation in DME, and better than laser photocoagulation alone.

Keywords: DME, PSTA, IVTA, CMT, BCVA.

INTRODUCTION

Although the ETDRS showed that scatter laser panretinal photocoagulation (PRP) decreased the incidence of severe vision loss in individuals with high-risk PDR, DR remains a major cause of blindness. The primary cause of acute visual disruption, macular oedema, can occasionally be caused or made worse by PRP, even though it may stop or inhibit growth in damaged retinas [(1)].

The primary cause of vision impairment in diabetics is macular edema. According to the ETDRS group's observations, DME has been categorized as clinically relevant if distinct, well-defined clinical characteristics are linked to either definite hard exudates in the macula's center or retinal thickening at or within one disc diameter of it. Focal laser photocoagulation has been shown to have a definite advantage for this subset of individuals. However, researchers are looking for alternative treatments for the management of DME because it is rare for clinically significant visual acuity recovery to occur, as well as for DME to recur or persist after appropriate laser treatment, especially in eyes that present angiographically with diffuse macular edema [(2)].

A synthetic glucocorticoid is triamcinolone. IVTA injections have been demonstrated to decrease macular thickness and enhance visual acuity in eyes with DME [(3)]. Ophthalmologists have lately utilized it as an intravitreal agent as an adjuvant therapy for DME in conjunction with retinal photocoagulation. Nevertheless, the remarkable outcomes of IVTA were not without adverse effects, including increased intraocular pressure (IOP), cataract development, unintentional intraocular infection (infectious endophthalmitis), retinal detachment, and traumatic cataract. These complications necessitate the use of a supplemental procedure to achieve the same outcome with fewer complications. Because of this, it has been suggested that a single posterior sub-tenon injection of PSTA be administered as an adjuvant before to retinal photocoagulation [(4)].

According to reports, blepharoptosis, orbital fat atrophy, strabismus, and conjunctival necrosis are possible side effects of PSTA [(5)]. The primary disadvantages of intravitreal injections include the possibility of retinal toxicity, the invasive nature of the procedure, the requirement for repeated injections, and the danger of endophthalmitis, despite studies indicating no toxicity of the IVTA injection [(6, 7)]. For several years, non-infectious uveitis has been successfully treated with periocular steroid injections [(8, 9)]. This study aimed to evaluate the effectiveness of PSTA versus IVTA before retinal photocoagulation on the final BCVA in DME. In addition to monitoring the impact of triamcinolone acetonide before laser photocoagulation in both directions on reducing the amount of macular thickening (edema) identified by fluorescein angiography and OCT. Additionally, it was to track how triamcinolone acetonide affected the growth of cataracts and IOP, as well as to report any additional complications.

PATIENTS AND METHODS

Patients: A randomized interventional comparative clinical trial conducted at the Outpatient Clinic of Ahmed Maher Teaching Hospital. This study included

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three groups; each included 20 eyes, all of which had clinically significant DME (CSDME) with focal or diffuse leakage in FFA.

Group I: 20 eyes treated with intravitreal injections of 4mg triami-cinolone acetate, followed by focal or grid laser treatment and PRP if needed in severe non proliferative or PDR 4 weeks later.

Group II: 20 eyes treated with posterior subtenon injection of 40 mg triamcinolone acetate, followed by focal or grid laser treatment and PRP if needed in severe non proliferative or PDR 4 weeks later.

Group III: 20 eyes treated with focal or grid laser treatment and PRP if needed in severe non proliferative or PDR.

Methods: All patients were subjected to the following, before and after treatment:

1- Measurement of BCVA

The illiterate E chart was used to test visual acuity before and after treatment. Sometimes BCVA were measured by the use of Snellen charts and Landolt Broken Ring Chart and converted to Log MAR decimal fraction for easy statistical analysis as the following:

- 6/6 =1
- 6/9 = 0.667
- 6/12 = 0.500
- 6/18 = 0.333
- 6/24 = 0.250
- 6/36 = 0.167
- 6/60 = 0.100
- 5/60 = 0.083
- 4/60 = 0.067
- 3/60 = 0.050
- 2/60 = 0.033
- 1/60 = 0.017
- Counting fingers at 50 cm = 0.008

2- Slit lamp examination, and complete anterior segment evaluation.

3- IOP assessment (Goldmann applanation tonometer).

4-Fundus examination and biomicroscopy using indirect ophthal-moscopy using Keeler® indirect ophthalmoscope using a Volk® 20 diopter lens for examining the peripheral retina and biomicro-scopy by a Volk® 90 diopter lens.

5-FFA to evaluate the perifoveal capillary network and exact points of leakage.

6- Evaluation of retinal thickness using topcon 3D OCT.

Inclusion Criteria:

1. Type I & II DM NPDR or PDR.
2. Normal IOP.
3. Systemically controlled diabetes, blood pressure, and other associated conditions.
4. FA showing diffuse or cystoid macular edema.
5. Central macular thickness more than 300 µm by OCT.

Exclusion Criteria:

1. Patients with media opacities and vitreous haemorrhage precluding proper fundus examination.
2. Patients with vitreomacular traction.
3. Patients with ischemic maculopathy area more than one disc diameter in FFA.
4. Previous treatment for DR in the form of LASER (focal or panretinal), intravitreal injections (within the last 6 months), or vitrectomy.
5. Uncontrolled ocular inflammation, posterior synechia, high IOP (glaucoma or ocular hypertension), or other ocular disease.
6. Uncontrolled systemic conditions such as DM, hyper-tension, renal disease, or bleeding tendency.

Technique:

Group I: was injected 0.1 ml of 40 mg/1 ml of intravitreal triamcinolone acetonide followed 1 month later by focal or grid & PRP laser therapy.

Group II: was injected with 1 ml of 40 mg/1 ml of posterior subtenon triamcinolone acetonide followed 1 month later by focal or grid & PRP laser therapy.

Group III: was treated by focal or grid laser photocoagulation & PRP if needed in severe non proliferative or PDR.

LASER technique:

Focal or grid LASER: was guided by FFA after intravitreal injections.

Type of LASER used: Argon laser.

Spot size: 50-100 micrometers, focal laser, no closer than 500 micrometers from the fovea

Power: Subtle gentle whitening on the leakage sites at the macula. In cases of severe NPDR and PDR the panretinal photo-coagulation (PRP) is performed (three sessions at 1-week interval). With the fundus laser lens and the argon laser installed on a slit lamp, the application took 0.1 seconds, the spot size on the retina was 200–300 micrometers, and the laser's initial strength was 150–200 mW to create a light intensity burn. Since there were around 500 locations in each session, there were roughly 1600 burns overall when the four sessions were over. In every situation, topical anesthetic is used. At the initial PRP session, focused or grid laser treatment is used if CSME was detected in the eyes at baseline.

Follow-up plan:

All patients were followed up as follows:

1. Visual acuity testing (BCVA).
2. Full slit lamp examination.
3. Measurement of IOP.
4. Fundus examination.
5. Fundus flurescein angiography FFA if needed.
6. Optical coherence tomography OCT at 1 week, 1 months, 3 months and 6 months intervals.

Timing:

1. Second day post injection, to exclude any side effects or complications of intravitreal injection and posterior subtenon injection.
2. One- and four-weeks post injection.
3. After three months, the last follow up is at six months from the injection date.

During the follow up sessions the following was performed:

1. Checking the response of the macular edema to the treatment, and looking for the favorable response of triamcinolone acetanoid by the after mentioned clinical examination and imaging techniques.
2. Recording the response macular edema to LASER.
3. Assessing the success rate and duration of response, i.e., dry macula, and its persistence over a period of six months from initial treatment.
4. Looking out for the complications of intravitreal injections such as lens injury, endophthalmitis, retinal injury and breaks, hemorrhage, elevated IOP, and complicated cataract.
5. Looking out for the complications of posterior subtenon injections such as muscle injury, ptosis, orbital fat atrophy and globe perforation.

Ethical approval: This study was approved by Ahmed Maher Teaching Hospital of Medicine's Ethics Committee. Following receipt of all information, signed consent was provided by each participant. The study adhered to the Helsinki Declaration throughout its execution.

Statistical analysis

Microsoft Excel and SPSS for Windows accomplished this. Quantitative variables were described using mean ± SD. Qualitative variables were described using percentages and numbers. To test the likelihood (P value), use the Student's t-test and the X^2-test. Statistical insignificance was defined as $P \leq 0.05$. Statistical significance is defined as $P<0.05$.

RESULTS

Our study involved 60 patients with clinically severe DME (non-ischemic type), in patients with type I & II DM, and who were in the NPDR and PDR stages. Twenty patients were included in group one (intravitreal and argon laser), twenty in group two (posterior subtenon and argon laser), and twenty in group three (argon laser only). The ages in group 1 ranged from 40 to 55 years with a mean of 48.94 ± 8.92, while the ages in group 2 ranged from 27 to 52 years with a mean of 47.62±9.60 and group 3' ages aged from 42 to 60 years with a mean of 51.39 ± 9.12. Fifteen males (75%) were enrolled in group 1, versus fourteen males (70%) in groups 2 and thirteen males (65%) in group 3, while females were 5 (25%) versus 6 (30%) and 7 (35%) in groups 1, 2 & 3 respectively.

According to type of diabetes: (type I DM) 5 (25%) were enrolled in group I, versus 8 (40%) in group II and 6 (30%) in group III, while (type II DM) 15 (75%) versus 12 (60%) and 14 (70%) in groups I, II & III respectively (Table 1).

Table (1): Distribution of the studied patients in group I, II & III regarding their age, sex and type of diabetes

Age		**Intravitreal + Laser**	**Sub-tenon + Laser**	**Laser only**	
Range		40 – 55	27 – 52	42 – 60	
Mean + SD		48.94 ± 8.92	47.62 ± 9.60	51.39 ± 9.12	
F. test		**2.215**			
p. value		**0.385**			
Sex		**Intravitreal + Laser**	**Subtenon + Laser**	**Laser only**	**Total**
Male	**N**	15	14	13	42
	%	75.0%	70.0%	65.0%	70.0%
Female	**N**	5	6	7	18
	%	25.0%	30.0%	35.0%	30.0%
Total	**N**	20	20	20	60
	%	100.0%	100.0%	100.0%	100.0%
Chi-square	**X^2**	**0.483**			
	P-value	**0.788**			
Type of DM		**Intravitreal + Laser**	**Sub-tenon + Laser**	**Laser only**	**Total**
DM Type I	**N**	5	8	6	19
	%	25.0%	40.0%	30.0%	31.7%
DM Type II	**N**	15	12	14	41
	%	75.0%	60.0%	70.0%	68.3%
Total	**N**	20	20	20	60
	%	100.0%	100.0%	100.0%	100.0%
Chi-quare	**X^2**	**1.082**			
	P-value	**0.583**			

Visual acuity (BCVA) (Table 2):

Assessment of visual acuity in group I: At **one week** 17 patients BCVA improved and 3 patients deteriorated, at **one-month** BCVA was improved in 18 patients and deteriorated in 2 patients, at **three months** BCVA was improved in 19 patients and deteriorated in 1 patient and at **final follow up visit** at 6 months BCVA was improved in 17 patients and deteriorated in 3 patients.

Assessment of visual acuity in group II: At **one week** 15 patients BCVA improved and 5 patients deteriorated, at **one-month** BCVA was improved in 18 patients and deteriorated in 2 patients, at **three months** BCVA was improved in 19 patients and deteriorated in 1 patient, and at final **follow up visit** at 6 months BCVA was improved in 16 patients and deteriorated in 4 patients.

Assessment of visual acuity in group III: At **one week** 12 patients BCVA improved and 8 patients deteriorated, at **one-month** BCVA was improved in 13 patients and deteriorated in 7 patients, at **three months** BCVA was improved in 14 patients and deteriorated in 6 patients and at **final follow up visit** at 6 months BCVA was improved in 11 patients and deteriorated in 9 patients.

Table (2): Comparison between the studied groups regarding their BCVA

Visual acuity			Intravitreal + Laser	Sub-tenon + Laser	Laser only	X^2	P-value
1 week	Improved	N	17	15	12	3.243	0.198
		%	85.0%	75.0%	60.0%		
	Not improved	N	3	5	8		
		%	15.0%	25.0%	40.0%		
1 month	Improved	N	18	18	13	5.569	0.062
		%	90.0%	90.0%	65.0%		
	Not improved	N	2	2	7		
		%	10.0%	10.0%	35.0%		
3 months	Improved	N	19	19	14	7.209	0.027*
		%	95.0%	95.0%	70.0%		
	Not improved	N	1	1	6		
		%	5.0%	5.0%	30.0%		
6 months	Improved	N	17	16	11	5.279	0.071
		%	85.0%	80.0%	55.0%		
	Not improved	N	3	4	9		
		%	15.0%	20.0%	45.0%		

* Significant.

In comparing every group individually, between pretreatment BCVA to post treatment BCVA after 6 months, there was significant improvement in groups I and II (P value equal 0.001). On the other hand, there was no significant improvement in group III in comparing the pretreatment BCVA and after 6 months follow up with p value equal 0.109 (Table 3).

Table (3): Comparison between the studied groups (log MAR) regarding their BCVA

Visual acuity		Intra-vitreal + Laser	Sub-tenon + Laser	Laser only	F. test	p. value	P1	P2	P3
Visual acuity pre	Range	0.1-0.4	0.1-0.3	0.1-0.3	0.853	0.524	0.358	0.649	0.651
	Mean±SD	0.23±0.18	0.19±0.13	0.21±0.14					
Visual acuity post 1 week	Range	0.2-0.5	0.2-0.4	0.1-0.3	7.664	0.001	0.462	0.001	0.004
	Mean±SD	0.34±0.09	0.32±0.08	0.24±0.07					
Visual acuity post 1 month	Range	0.2-0.6	0.2-0.5	0.1-0.4	8.256	0.001	0.416	0.001	0.002
	Mean±SD	0.39±0.13	0.37±0.12	0.26±0.09					
Visual acuity post 3 months	Range	0.3-0.7	0.3-0.6	0.2-0.4	9.354	0.001	0.389	0.001	0.001
	Mean±SD	0.51±0.15	0.47±0.14	0.29±0.12					
Visual acuity post 6 months	Range	0.3-0.6	0.3-0.5	0.2-0.4	9.578	0.001	0.419	0.001	0.001
	Mean±SD	0.49±0.16	0.45±0.15	0.28±0.13					
P. value pre & post 6 months		0.001*	0.001*	0.109					

* Significan, P1 = Intravitreal + Laser & Sub-tenon + Laser, P2 = Intravitreal + Laser & Laser only, P3 = Sub-tenon + Laser & Laser only.

Central macular thickness assessment: (table 4)

Assessment of central macular thickness in group I: At **one week** 18 patients CMT improved and 2 patients did not improve, at **one-month** CMT improved in 18 patients and did not improve in 2 patients, at **three months** CMT improved in 17 patients and did not improve in 3 patients and at **final follow up visit** at six months CMT improved in 16 patients and did not improve in 4 patients.

Assessment of central macular thickness in group II: At **one week** 16 patients CMT improved and 4 patients did not improve, at **one-month** CMT improved in 18 patients and did not improve in 2 patients, at **three months** CMT improved in 19 patients and did not improve in 1 patient and at **final follow up visit** at six months CMT improved in 17 patients and did not improve in 3 patients.

Assessment of central macular thickness in group III: At **one week** 12 patients CMT improved and 8 patients did not improve, at **one-month** CMT improved in 13 patients and did not improve in 7 patients, at **three months** CMT improved in 14 patients and did not improve in 6 patients and at **final follow up visit** at six months CMT improved in 11 patients and did not improve in 9 patients.

Table (4): Comparison between the studied groups regarding their CMT regression

CMT			Intravitreal + Laser	Sub-tenon + Laser	Laser only	X^2	P-value
1 week	**Improved**	N	18	16	12	**5.221**	**0.074**
		%	90.0%	80.0%	60.0%		
	Not improved	N	2	4	8		
		%	10.0%	20.0%	40.0%		
1 month	**Improved**	N	18	18	13	**5.569**	**0.062**
		%	90.0%	90.0%	65.0%		
	Not improved	N	2	2	7		
		%	10.0%	10.0%	35.0%		
3 months	**Improved**	N	17	19	14	**4.562**	**0.102**
		%	85.0%	95.0%	70.0%		
	Not improved	N	3	1	6		
		%	15.0%	5.0%	30.0%		
6 months	**Improved**	N	16	17	11	**5.283**	**0.071**
		%	80.0%	85.0%	55.0%		
	Not improved	**N**	4	3	9		
		%	20.0%	15.0%	45.0%		

Central macular thickness regression (mean ± SD) in µm: In comparing every group individually, between pretreatment CMT to post treatment CMT after 6 months, there was significant improvement in the groups I (P value equal 0.002) and II (P value equal 0.001). On the other hand, there was no significant improvement in group III in comparing the pretreatment CMT and after 6 months follow up with p value equal 0.365 (Table 5).

Table (5): Comparison between the studied groups numbers regarding their CMT in microns

CMT	Intra-vitreal + Laser	Sub-tenon + Laser	Laser only	F. test	p. value	P1	P2	P3
	Mean + SD	Mean + SD	Mean + SD					
Pre treatment	410.65 ± 120.74	418.95 ± 135.62	408.93 ± 108.65	**2.245**	**0.335**	0.486	0.369	0.284
Post treatment								
1 week	345.69 ± 68.65	341.25 ± 85.67	394.21 ± 64.95	**3.341**	**0.036***	0.711	0.034*	0.027*
1 month	328.27 ± 85.64	311.61 ± 88.94	384.82 ± 82.37	**4.023**	**0.024***	0.549	0.039*	0.010*
3 months	280.36 ± 84.67	276.67 ± 92.78	374.68 ± 94.86	**0.965**	**0.596**	0.898	0.002*	0.003*
6 months	293.92 ± 93.37	279.47 ± 93.64	378.18 ± 103.24	**0.568**	**0.802**	0.628	0.010*	0.006*
p. value pre & post 6 months	0.002*	0.001*	0.365					

* Significan, P1 = Intravitreal + Laser & Sub-tenon + Laser, P2 = Intravitreal + Laser & Laser only, P3 = Sub-tenon + Laser & Laser only.

Complications:

1) IOP:

IOP after treatment assessment: (table 6)

Assessment of IOP in group I: At one week, the IOP did not change for four patients and increased for sixteen; at 1 month, it did not change for seven patients and increased for thirteen, at 3 months, it did not change for twelve patients and increased for eight and at the final follow-up visit at 3 months, it did not change for nineteen patients and increased for one.

Assessment of IOP in group II: At one week, fourteen patients' IOP did not change, while six patients did. At 1 month, sixteen patients' IOP did not change, and four patients did. At 3 months, eighteen patients' IOP did not change, and two patients did. At the final follow-up visit at 6 months, none of the twenty patients' IOPs decreased.

Assessment of IOP in group III: At **one week**, **one month**, **three months** and **All 20 patients' IOPs were unchanged at the final follow-up appointment six months later.**

P value is < 0.005 after one week < 0.005 after one month, < 0.005 after three months and < 0.005 after six months. So, there was significant change between the three groups.

Table (6): Comparison of the members studied groups regarding their IOP after treatment

IOP			Intravitreal + Laser	Sub-tenon + Laser	Laser only	X^2	P-value
1 week	No change	N	4	14	20	28.130	0.001*
		%	20.0%	70.0%	100%		
	Increased	N	16	6	0		
		%	80.0%	30.0%	0.0%		
1 month	No change	N	7	16	20	21.827	0.001*
		%	35.0%	80.0%	100%		
	Increased	N	13	4	0		
		%	65.0%	20.0%	0.0%		
3 months	No change	N	12	18	20	12.479	0.002*
		%	60.0%	90.0%	100%		
	Increased	N	8	2	0		
		%	40.0%	10.0%	0.0%		
6 months	No change	N	19	20	20	2.028	0.362
		%	95%	100%	100%		
	Increased	N	1	0	0		
		%	5.0%	0.0%	0.0%		

* Significan, No change: changes within two mmHg.

In comparing every group individually, between pretreatment IOP to post treatment IOP after 6 months, there was significant change in group I (P value equal 0.012). On the other hand, there was no significant change in groups II (P value equal 0.761) and III (P value equal 0.881) in comparing the pretreatment IOP and after 6 months follow up (table 7).

Table (7): Comparison between the three studied groups regarding their IOP in mmHg

IOP	Intra-vitreal + Laser	Sub-tenon + Laser	Laser only	F. test	p. value	P1	P2	P3
	Mean + SD	Mean + SD	Mean + SD					
Pre treatment	15.21±2.65	14.53± 2.42	15.17±2..36	**0.847**	**0.402**	0.365	0.542	0.423
Post treatment								
1 week	23.15 ± 3.65	18.53 ± 2.84	15.19 ± 2.45	**7.473**	**0.001***	0.001*	0.001*	0.001*
1 month	21.82 ± 3.28	17.04 ± 2.75	15.15 ± 2.31	**7.039**	**0.001***	0.001*	0.001*	0.024*
3 months	19.59 ± 3.23	15.86 ± 2.68	14.96 ± 2.18	**4.935**	**0.003***	0.001*	0.006*	0.251
6 months	18.21 ± 3.17	14.79 ± 2.92	15.06 ± 2.27	**4.208**	**0.009***	0.001*	0.008*	0.746
p. value pre & post 6 months	0.012*	0.761	0.881					

* Significan.

Table (8) showed that it was clearly noticeable that IVTA had a detrimental effect on the lens with advances in both the rate and degree of cataract progression, this was in contrary to the PSTA & Laser groups, which showed only minimal changes and no changes respectively in lens status throughout the study.

Table (8): Demonstrating changes in lens status in the three groups

Follow up	Intravitreal + Laser	Sub-tenon + Laser	Laser only
Preoperative data:			
Cortical %	0 cases	0 cases	0 cases
Nuclear sclerosis %	10% (2 cases)	15% (3 cases)	10% (2 cases)
PSC %	5% (1 case)	5% (1 case)	0 cases
1 month			
Cortical %	5% (1 cases)	0 cases	0 cases
Nuclear %	15% (3 cases)	15%(3 cases)	10% (2 cases)
PSC %	10% (2 cases)	5% (1 case)	0 cases
3 months			
Cortical %	5% (1 cases)	0 cases	0 cases
Nuclear %	20% (4 cases)	15%(3 cases)	10% (2 cases)
PSC %	20% (4 cases)	5% (1 case)	0 cases
6 months			
Cortical %	5% (1 cases)	0 cases	0 cases
Nuclear %	20% (4 cases)	15%(3 cases)	10% (2 cases)
PSC %	20% (4 cases)	5% (1 case)	0 cases

DISCUSSION

This study included three groups; each included 20 eyes, all of which had clinically significant DME (CSDME) with focal or diffuse leakage in FFA. **Group I:** 20 eyes treated with intravitreal injections of 4mg triamicinolone acetonide, followed by focal or grid laser treatment and PRP if needed in severe non proliferative or PDR 4 weeks later, **Group II:** 20 eyes treated with posterior subtenon injection of 40 mg triamicinolone acetonide, followed by focal or grid laser treatment and PRP if needed in severe non proliferative or PDR 4 weeks later, and **Group III:** 20 eyes treated with focal or grid laser treatment and PRP if needed in severe non proliferative or PDR.

The efficacy of groups I, II, and III in treating DME was compared in this study. During the first three months of therapy, DME reacted effectively both anatomically and functionally to IVTA group I and PSTA group II injections and laser; however, the decrease in CMT following IVTA injections was noticeably more pronounced than following PSTA injections. The visual acuity increase was also improved and stabilized in the PSTA group, but it was more noticeable in the IVTA group during the first three months. However, following the next follow-up, the results showed a gradual increase in CMT in both groups, which is more noticeable in the IVTA group. This difference was not statistically significant. In contrast to clinical research, **Sumit and Dennis** [(10)] found that IVTA injection greatly reduced leakage caused by photocoagulation-induced blood retinal barrier breakdown, whereas PSTA administration did not. Our work has revealed that PSTA injection with sequential laser photocoagulation appeared to be successful for the treatment of DME both functionally (defined by visual acuity) and physically (determined by CMT).

The treatment impact on CMT is greater than that on visual acuities in both the IVTA and PSTA groups, but the third group (laser alone) appeared to have a much more stabilizing rather than enhancing effect on visual acuity. We propose that the lack of visual acuity to improve completely despite improvement in retinal thickness may be related to retinal inner and outer segment damage induced by persistent macular edema. When IVTA was used as a therapy for diffuse DME, most patients showed improvements in BCVA and CMT at early intervals (1 week to 1 month) after injection; however, in some cases, these improvements declined 3 to 6 months after injection. And the results regarding improvement of CMT were established at early intervals (1 week to 1 month) in most of the cases and there was a little improvement (1month to 3 months) then decreased at late intervals at (3 to 6 months) post injection. On the other hand, on using PSTA as a treatment for diffuse DME, results regarding improvement of BCVA and improvement of CMT were established at late intervals (1 to 3 months) post injection in most of the cases and still improving reaching the maximum improvement at the 6th month in many of the cases. And the results regarding improvement of CMT were established at late intervals (1 to 3 months) then still improving till the 6th month post-injection but at slower rate. That showed a prolonged effect than that of intravitreal group.

Probable complications of injections with corticosteroids include retinal detachment, vitreous hemorrhage, endophthalmitis, cataract development or progression, and elevated IOP. The greatest IOP rise in the current research was 18.53 mmHg in PSTA and

23.15 mmHg in IVTA. With the exception of one instance in group one, where optic nerve damage necessitated vitrectomy to remove the remaining IVTA, practically all of the patients could be managed with topical anti-glaucoma medication. According to one author, the steroid-induced rise in IOP would not be a significant contraindication for using IVTA injections to treat neovascular and edematous ocular disorders [(11)]. For the treatment of DME in individuals with known glaucoma, PSTA may be a better option than IVTA. None of the diabetic patients experienced any systemic adverse effects, despite the fact that we lack sufficient information on the systemic effects of triamcinolone acetonide injection. Even though IVTA injections appear to be safe, endophthalmitis can develop more easily in diabetics, therefore one should constantly be on the lookout for it. It is important to remember that PSTA injection, as opposed to IVTA injection, may be a less intrusive and safer method for treating DME. Perforation of the globe and accidental injection into the choroidal or retinal circulation are two additional possible risks associated with periocular injections [(8, 9)].

The primary drawback of PSTA is that during the early follow-up period for the treatment of DME, its effects were not as significant as those of IVTA. Both PSTA and IVTA significantly improved visual acuity and reduced CMT regression in the current investigation, particularly in the short-term. Though less dramatic than IVTA injections, PSTA injections also appeared to be a safe and effective method for treating DME. IVTA injections were more successful and produced more dramatic responses [(9)]. **Veritti *et al.*** [(12)] increased the impact of the PSTA injection by altering its formula and adding specific chemicals to extend its effect and avoid reflux during the triamcinolone acetonide PSTA, such as 20 mg sodium chondroitin sulfate and 15 mg sodium hyaluronate (1.5 mL).

In our study regarding BCVA and CMT:

In Group (I) IVTA: In contrast to **Ozdek *et al.*** [(13)] and **Lam *et al.*** [(14)] who found that the IVTA group showed a dramatic response to the treatment in the early period and that this response began to diminish after the third month, our study supports their findings. However, they reported that the response to the treatment after three months was nearly completely eliminated at the sixth month, when the visual acuity values returned to baseline, even though the CMT values were still significantly lower than the baseline. According to our research, there was a relationship between increased visual acuity and decreased macular thickness, particularly between the third and sixth months following intravitreal injection. It was noticed that the visual acuity started to decrease with the macular thickness slight progression to increase.

In our study, visual acuity improved initially until one and three months after intravitreal injection and laser, and then it declined again three to six months after intravitreal injection. These findings are almost identical to those of **Jonas *et al.*** [(15)] who found that the improvement in visual acuity was not consistent throughout the study's follow-up period and that visual acuity tended to decline about five months after the intravitreal injection. According to **Kaur *et al.*** [(16)], both IVTA and PSTA resulted in a statistically significant decrease in the degree of macular edema at each follow-up visit one, two, and three months after injection. However, when compared to PSTA, IVTA resulted in a larger decrease in CMT and an improvement in visual acuity at every visit. The two groups' differences were statistically significant, which contradicts our study. Although they concluded that PSTA is less effective than IVTA but IVTA is producing much more elevation in IOP. The research conducted by **Tufan *et al.*** [(17)] to assess the effectiveness of IVTA and IVTA with macular laser grid photocoagulation treatment in diffuse DME revealed the same results as our study for group I at the 6-month follow-up. The outcomes matched those of our study, however an assessment of IVTA-related complications and the need for reinjection revealed that, on average, 7 ± 4months after the initial injection, 55% of the control group and 66% of the laser groups required reinjection. There was a 33% increase in IOP and a 22% advancement in cataracts.

In our study regarding BCVA and CMT:

In Group (II) PSTA: In our study the effect of PSTA injection augmented with argon laser seemed to increase slowly till 1 month then rapidly increased at 3 months till 6 months after PSTA. This is more than that reported by **Ozdek *et al.*** [(13)], which included 85 eyes of 60 patients in the PSTA group. The study reported that the effect of PSTA injection seemed to last at least about 3 months. Our study is in agreement with that of **Bakri and Kaiser** [(18)], who revealed that It has been demonstrated that giving individuals with DME 40 mg PST injection helps to stabilize or improve their visual acuity. Our study revealed that individuals undergoing injections of posterior sub-tenon triamcinolone for DME had improved eyesight. The study by **Entezari *et al.*** [(19)], which was conducted on 63 eyes of 50 patients who received a 40 mg posterior subtenon injection, showed stabilization and improvement in vision. It also recorded a slight, temporary increase in IOP at 3 months, which can be easily controlled. This study is somewhat different from ours, which recorded an increase in IOP at 1 week until the first month.

In our study, the decrease in macular thickness was substantial following IVTA and PSTA injections at the end of the follow-up period. However, the decrease in macular thickness was greater in the IVTA group at one week, one month, and three months, while the PSTA group improved more in the sixth month. This is consistent with a study by **Ozdek *et al.***

[13], using 41 eyes from 35 patients in the IVTA group who received 4 mg/0.1ml triamcinolone acetonide and 85 eyes from 60 patients in the PSTA group who received only 20 mg/0.5ml triamcinolone acetonide, they revealed that DME responded well anatomically and functionally to both PSTA and IVTA injection during the first three months of treatment, but that the decrease in macular thickness was noticeably more pronounced following IVTA injection, supporting PSTA as an IVTA substitute.

In Group (III) laser only: Our results agree with the results of **Verma *et al.*** [20] who evaluated posterior subtenon triamcinolone's adjuvant function in the treatment of diffuse DME. A total of 31 DME-affected eyes were split into two groups: One that received grid laser photocoagulation and 0.5 mL of 40 mg/mL posterior subtenon triamcinolone, and the other that received grid laser photocoagulation alone. At presentation and six, twelve-, and twenty-four weeks following intervention, BCVA, contrast sensitivity, and IOPs were measured. The mean BCVA of the interventional group increased from 20/160 to 20/100 (two-line rise on ETDRS) ($p=0.024$), which was statistically significant ($p<0.05$). None of the patients in either group showed a notable increase in IOP. An effective and secure supplement to the standard treatment of DME is the injection of posterior subtenon triamcinolone. **Shima *et al.*** [21] studied the impact of a 20 mg PSTA injection of TA alone visual acuity (VA), CMT as calculated by OCT, and the retina's fluorescein angiographic appearance were the primary outcome measures employed one to two months prior to focal photocoagulation. At least six months were spent monitoring the patients. They discovered that the CMT improved significantly for up to six months, and that 37.5% of patients had satisfactory visual outcomes at six months. Additionally, none of the patients showed a decline in VA. These results are agreeing with our results as for the dose difference and its effect on trans-scleral absorption of TA. The impact of PSTA is dose-dependent, and its pharmacokinetics include TA diffusing through the sclera to reach the retina. When medication reflux happened, the real amount of TA was less than an effective dosage, even though the PSTA utilized in this trial was 40 mg. According to reports, vitreous drug concentrations ranged widely, from 0 to 4.93μm/ml, even with 40 mg of PSTA [11, 22, 23].

As regard to IOP, cataract and other complications: In our study, thirty percent (6 cases) of the PSTA group and eighty percent (16 cases) of the IVTA group experienced a substantial increase in IOP after one week as compared to the pretreatment time. Despite the fact that the second group's elevation was not greater than 21 mmHg, this consequence was observed to happen less frequently following PSTA injection. According to **Ozdek *et al.*** [24] and the studies of **Nozik** [8] and **Helm and Holland** [9], a rise in IOP of more than 21 mmHg was seen in 24.3% of the IVTA group and 8.2% of the PSTA group. This is virtually identical to the work of **Bakri and Kaiser** [18], who saw a modest, temporary rise in IOP over three months that was readily managed. Nevertheless, our investigation documented an IOP rise from one week to the first month. Significant IOP increases were recorded in up to 50% of the eyes following IVTA administration [6, 11, 25, 26]. However, all instances are managed with topical antiglaucomatous medication. Additionally, our findings on PSTA safety are comparable to those of **Byun and Park** [27], who assessed the increase in IOP in 18 out of 159 eyes from 158 patients who received 40 mg (1.0 ml) of PSTA. Due to an elevated IOP following injection, 18 out of 159 eyes in that trial needed glaucoma medication.

CONCLUSION

- While both IVTA and PSTA injections resulted in a notable improvement in visual acuity and a decrease in CMT, the IVTA group experienced a more noticeable effect, particularly in the short term. In the long run, however, PSTA injection also appeared to be a safer and more effective method of enhancing the effects of argon laser treatment for DME.
- Comparing grid laser alone to the other two treatment techniques, the former was noticeably poorer.
- IVTA injections' primary complication was steroid-induced ocular hypertension, which was often manageable with topical antiglaucoma combo remove this drugs. One main contraindication is such an incident. Because of the significant risk of IOP increase following injection, patients need to be closely watched.

RECOMMENDATIONS

Managing DM is the initial step in treating DR. Maintaining control over the diabetic condition is necessary, and lowering the severity of DR also requires controlling or removing recognized risk factors.

Recommendations for treatment of DME: At the final of the study the results of both types of injection (IVTA & PSTA) are comparable as an adjunctive treatment with argon laser photocoagulation of DME especially when Anti-VEGFs are not preferred, but we advise the subtenon route to decrease the risk of complications. Also, we recommend PSTA for cases suspected to be glaucomatous. It is not recommended to perform macular focal or grid laser alone as a sole treatment of DME.

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