

DIABETIC MACULAR OEDEMA AND ROLE OF INTRA VITREAL TRIAMCINOLONE ACETONIDE

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ABSTRACT

Aims: The aim of this study was to determine efficiency of intravitreal injection of triamcinolone (IVT) in diffuse macular edema secondary to diabetes mellitus.

Methods: Twenty eight eyes of 28 patients who fulfilled the inclusion criteria were selected for the study. Patients had a full ophthalmic examination carried out. Injection triamcinolone acetonide (Kenalog) was given intravitreally with full aseptic measures patients were followed up at selected intervals of time.

Results: At one month post injection interval 54% patients showed improvement in visual acuity. Three months post injection 43% patients maintained improvement in visual acuity. At six months post injections 18% maintained improvement while 43% showed no change and 14% showed deterioration of vision.

Conclusion: We conclude that IVT has a favorable outcome in significant number of patients and may be an alternative to laser photocoagulation in diffuse macular edema secondary to diabetes mellitus.

Keywords: Diabetic macular edema, intravitreal triamcinolone, raised intraocular pressure, endophthalmitis.

INTRODUCTION

Diabetic retinopathy (DR) is the leading cause of new blindness in working population with 135 million individuals affected across the world. Diabetic macular edema (DME) is a manifestation of DR that produces loss of central vision. Macular edema affects approximately 29 % of diabetic patients with disease duration of 20 years or more and main reason for reduced vision in this population [1]. There are two different types of DME. Focal edema which is due to focal leakage from microaneurysms resulting in lipid deposit of circinate pattern and diffuse macular edema which is due to diffuse leakage by retinal capillaries. In "early treatment diabetic retinopathy study (ETDRS) a 3 years risk of moderate visual loss (decrease of 3 lines of visual acuity (VA) chart) with clinically significant macular edema (CSME) was 30%. In ETDRS laser

photocoagulation (PC) reduced the risk of moderate visual loss with DME in mild to moderate DR by 50% [2].

In eyes with diffuse macular edema laser treatment cannot be focused on localized leaking microaneurysms since there is diffuse leakage from capillary bed and thickening of entire macula. Grid laser treatment covering the whole macular region with a net of small laser coagulation spots carries a particularly poor prognosis [3,4].

In view of fact that diffuse macular edema has poor response to laser PC and laser cannot be applied in leaks very close to foveal avascular zone (FAZ). Triamcinolone acetonide (TA) a corticosteroid suspension has been used in cystoid macular oedema (CMO) secondary to uveitis [5,6], exudative age related macular degeneration (ARMD) [7] and neovascular glaucoma [8], Proliferative diabetic retinopathy (DR) [9]. We undertook present study to assess if an intra vitreal injection would be effective in improving

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visual acuity in patients of DME unresponsive to laser photocoagulation (PC).

PATIENTS AND METHODS

Twenty eight eyes of 28 patients with CSME according to ETDRS criteria were treated between March 2005 and August 2006. This was a quasi-experimental study. All patients were fully informed and signed informed consent was taken. All patients were having DME which had received laser photocoagulation treatment at least 3 months before IVT and not responding or were unfit for laser photocoagulation (PC) due to leakage close to FAZ as determined by fundus fluorescein angiography (FFA). All patients had a regular follow up with controlled blood sugar levels to preclude possible effects of un-controlled blood sugar levels as an adverse factor for resolution of DME. Patients with associated central retinal vein occlusion (CRVO), branch retinal vein occlusion (BRVO), glaucoma uveitis and macular ischemia were excluded.

Examination carried out at base line and all patients received a complete eye examination including best corrected visual acuity. Applanation tonometry, slit lamp examination, dilated fundus examination of posterior pole with contact lens and status of retinopathy and macular edema was noted. Clinically Significant Macular Edema was defined according to ETDRS criteria. Fundus Fluorescein Angiography was done which showed diffuse macular leakage. All patients had their glycemic control assessed by Hb AC. Intra vitreal injection of triamcinolone acetonide (TA) was carried out under sterile conditions in operation theatre with topical anaesthesia. Topical anaesthesia was obtained using proparacaine eye drops soaked cotton tipped applicator followed by cleaning by 5% povidone iodine solution. Triamcinolone acetonide (Kenalog) was injected into vitreous cavity under operating microscope after pupillary dilatation infero temporally with a 27 gauge needle at dose of 4 mg in 0.1 ml. After injection patients were instructed to sit in up right position for one hour to prevent

crystals settling in macular region. Indirect ophthalmoscopy was used to confirmed intra vitreal location of suspension and the perfusion of optic nerve head. Retinal artery pulsations were noted. All patients were given topical beta blockers to control post IVT for rise of IOP. All patients were followed up at one week, and then one month, three months and six months. At each review best corrected Snellen visual acuity was noted along with status of retinopathy. FFA was performed to assess any decrease in leakage. All patients were monitored for injection related complications and those due to corticosteroid medication including Retinal Detachment (R.D), vitreous hemorrhage (VH), endophthalmitis, raised IOP and cataract.

RESULTS

Twenty eight patients were included in the research. Study sample consisted of 22 males (78.6%) and 6 females (21.4%). Male to female ratio was 3.67:1. The mean age of patients undergoing IVT was 60.57 years, ranging from 45 to 80 years. Mean duration of diabetes was 16.1 years ranging from 9 to 35 years (figure). 20 (71.4%) patients were on oral hypoglycemic medicines, 8 (29%) patients were using insulin. Mean duration of post-IVT follow-up was 8.32 months, ranging from 3 to 17 months 21 patients completed 6 months or more of follow-up. Three patients left follow-up after 3 months, one after 4 months and 3 patients after 5 months however 9 patients completed 1 year or more of follow-up. Out of 28 patients 20 (71%) had previous grid laser treatment and 8 (29%) could not have laser treatment by virtue of location of leakage site near to FAZ confirmed on FFA. At one month post-IVT 15 (54%) patients showed improvement in visual acuity. Eleven (40%) patients showed no change and 2 (7%) patients showed deterioration in VA by one line on Snellen's visual acuity chart. Nine patients showed improvement by 1 line. Five patients showed improvement by 2 lines and only one patient showed improvement by 3 lines on Snellen's Visual acuity chart (table). At 3 months after

the injection 12 (43%) patients maintained improvement in VA, 12 (43%) patients showed no change and 4 patients (14%) showed deterioration in VA by one line on Snellen's visual acuity chart. Ten patients maintained improvement by 1 line and 2 patients maintained improvement by 2 lines on Snellen's visual acuity chart (table). At 6 months after the injection 7 patients did not report for follow-up. Five (24%) patients maintained improvement in VA by one line, 12 (57%) patients showed no change and 4 (19%) patients showed deterioration in VA by one line on Snellen's visual acuity chart (table). Two patients developed sterile endophthalmitis and three patients showed rise in IOP despite topical beta-blockers after injection. No patients had traumatic cataract or retinal detachment.

DISCUSSION

For long time cortico steroids have been used in Ophthalmology. Cortisone in an intra vitreal form was earlier advocated by Machrever et al [10] for managing vitro-retinopathy. But fear was that of ocular toxicity. Experimental studies showed that triamcinolone acetonide was not toxic since then they have been used extensively in experimental trials in patients without no significant toxic effect [11]. The exact mechanism of cortiosteroids in treatment of macular edema is not known but certain rationale are given for their use such as their ability to inhibit the archidonic pathway of which Prostaglandin is a product, steroids is known to also decrease the production of VEGF [12] they also reduce the breakdown of blood retinal barrier [13] by reducing permeability of retinal capillaries by increase in number of and activity of tight junctions [14]. Since cortisone is washed out of eye within 24 hours of Intra vitreal injection [15] Machener advocated the use of depot form of steroids which have and Intra vitreal absorption time of about 2-5 month hence allowing a longer period of steroid contact than a single injection of cortisone [16].

The results of present study suggest that intra vitreal injection of triamcinolone acetonide (TA) is a useful tool in management of DME our patients showed there is a definite improvement in corrected visual acuity in resistant cases of DME. The most significant improvement in VA was noted in the first month post intra vitreal (54%) which was maintained in 43% at 3 months at six months post injections 18% maintained improvement while 43% showed no change and 14% showed deterioration of vision.

The results of this study confirm previous reports showing IVT can improve VA in diffuse DME. Adam Martidis et al [2] in their study reported of 16 eyes with CSME that failed to respond to previous sessions of laser photocoagulation in a follow up of 6 months showed a mean improvement in visual acuity of 2.4 and 1.3 Snellen lines at 1,3 and 6 months follow up alongwith decrease of central macular thickness (as measured by OCT) of 55%, 57% and 38% over same interval from the Initial Pre treatment levels. These results were later confirmed by other studies including that of Jonas JB [17] who evaluated outcome of IVT in diffuse diabetic macular edema and concluded that Intra vitreal triamcinolone acetonide resulted in improvement in VA with major side effects not being observed. They enrolled 26 eyes of 20 patients. Mean visual acuity improved from 0.12 at base line to 0.19 during follow up. FFA during pre injection and post injection periods showed a significant decrease in flourscein leakage after IVT. Ciardella AP [18] right came up with similar results including re-absorption of hard exudates present in macular over the follow up period. None of these studies experienced any major complications from IVT injection. The great fear of injecting intra vitreal steroids is that of complications due to steroids such as direct drug toxicity on retina and optic nerve, rise of IOP, cataract progressions and complications due to intravitreal injection such as RD, Vitreous hemorrhage and endophthalmitis which is a dreaded complication. All the studies have

Table: Changes in visual acuity following IVT injection.

Case	Age(Y)	Date of Injection	Follow-up(m)	VA Pre-IVT	VA 1 m	VA 3 m	VA 6 m
1	68	30.03.05	6	2/60	6/60	6/60	6/60
2	57	01.06.05	6	3/60	5/60	5/60	5/60
3	51	17.06.05	6	6/18	6/6	6/12	6/18
4	80	21.06.05	6	6/36	6/60	6/60	6/60
5	73	21.06.05	6	3/60	6/60	6/60	6/60
6	59	29.06.05	6	2/60	6/60	6/60	6/60
7	60	27.07.05	6	2/60	2/60	2/60	2/60
8	67	27.07.05	6	6/60	6/60	6/60	6/60
9	65	17.08.05	6	6/24	6/12	6/18	6/24
10	59	30.09.05	6	6/60	6/60	6/60	6/60
11	51	23.12.05	6	2/60	2/60	2/60	2/60
12	59.5	05.01.06	6	6/24	6/12	6/18	6/24
13	50	07.01.06	6	2/60	2/60	2/60	2/60
14	55	25.01.06	6	6/36	6/36	6/60	6/60
15	54	25.01.06	6	6/36	6/24	6/24	6/24
16	57	25.01.06	6	6/18	6/24	6/24	6/24
17	55	25.01.06	6	2/60	2/60	2/60	2/60
18	45	01.02.06	6	2/60	6/60	6/60	6/60
19	55	01.02.06	6	6/36	6/18	6/36	6/60
20	60.5	22.02.06	6	6/18	6/9	6/18	6/18
21	45	15.02.06	6	6/24	6/24	6/24	6/24
22	69	02.03.06	5	6/60	6/36	6/36	-
23	58	08.03.06	5	6/36	6/18	6/24	-
24	70	29.03.06	5	2/60	6/36	6/36	-
25	64	19.04.06	4	6/24	6/24	6/24	-
26	69	24.05.06	3	6/60	6/36	6/36	-
27	65	30.05.06	3	6/18	6/18	6/18	-
28	75	01.06.06	3	2/60	5/60	2/60	-

Key Legend: VA: Visual Acuity IVT: Intra Vitreal Triametholone Acetonide M: Months Y: Years

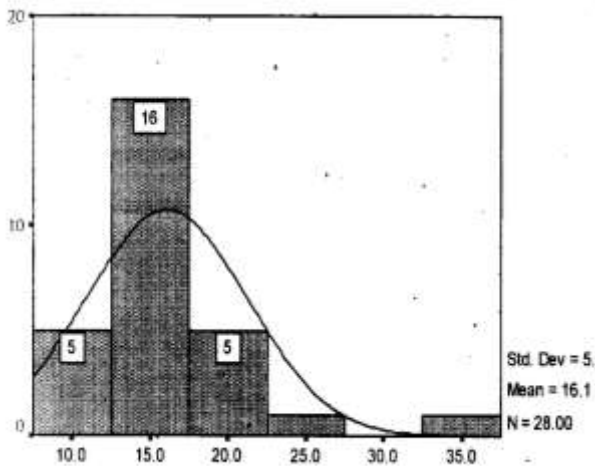


Figure: Duration of diabetes mellitus in various patients group.

observed that major side effects were not seen. In our study rise of IOP (exceeding 21 mmHg) which is lower than those of previous studies which showed 31-35mg [19] was observed in 3 patients despite use of anti-glaucoma medications. Two patients

developed sterile endophthalmitis which was managed with oral steroids. No patients showed progression of cataract. No Retinal detachment or vitreous hemorrhage was seen post injection.

CONCLUSION

Intra Vitreal triamcinolone acetonide is effective in improving visual acuity, best results are seen at maximum of 1-3 months after IVT injection. The improvement as early as 1 week after IVT has been observed but this is followed by decline in vision and increase in macular thickness over following months. We conclude that IVT for DME has favourable result in a significant number of patients with minimal side effects and hence may be an alternative of laser PC in a selective group of patients. This is in agreement with previous studies further research in a larger population needs to be done for establishing it as alternative to laser P-C.

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