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A COMPARATIVE STUDY OF EFFECTS OF INTRAVITREAL TRIAMCINOLONE ACETONIDE INJECTIONS OF DIFFERENT DOSES IN PATIENTS WITH DIABETIC MACULAR EDEMA

Ophthalomology

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ABSTRACT

Diabetic macular edema (DME) is a significant cause of visual impairment in individuals with diabetes. This prospective, randomized, comparative study aimed to assess the visual outcomes and complications associated with different doses (1mg, 2mg, and 4mg) of Intravitreal Triamcinolone Acetonide (IVTA) injection in patients with DME. A total of 75 patients were enrolled, and following clinical diagnosis, they were randomly assigned to receive one of the three IVTA doses. Visual acuity, intraocular pressure (IOP), cataract progression, and macular edema reduction were evaluated at various time points post-injection. The study found that visual acuity improvement was comparable between the 1mg and 2mg groups, showing 52% and 56% improvement, respectively. The 4mg group exhibited a slightly lower improvement rate of 40%. Fluorescein angiogram (FFA) results indicated that 68% of patients in the 2mg group showed improvement, while it was 60% in the 1mg group and 64% in the 4mg group. Optical coherence tomography (OCT) revealed a mean reduction in macular thickness of 59.28 micrometers in the 1mg group, 97.08 micrometers in the 2mg group, and 91.68 micrometers in the 4mg group. However, the study also observed significant complications associated with the higher 4mg dose. Patients in the 4mg group experienced a more pronounced rise in IOP, which peaked at the end of the first month post IVTA. Fortunately, IOP levels returned to normal by the end of three months with the help of topical antiglaucoma medications. Additionally, cataract progression was more prominent in the 4mg group compared to the 1mg and 2mg groups. In conclusion, this study suggests that administering a 4mg dose of IVTA does not yield significantly better outcomes than a 2mg dose in terms of DME improvement. On the contrary, the higher dose is associated with a higher risk of complications, including elevated IOP and accelerated cataract formation in phakic patients. Thus, a careful consideration of the dose is crucial when using IVTA to treat diabetic macular edema.

KEYWORDS

IVTA, FFA, macular edema

INTRODUCTION

Diabetic macular edema (DME) is the accumulation of excess fluid in the extracellular space within the retina in the macular area, typically in the inner nuclear, outer plexiform, Henle's fiber layer, and subretinal space[1][2]. DME can develop at any stage of diabetic retinopathy (DR), from mild nonproliferative diabetic retinopathy (NPDR) to proliferative diabetic retinopathy (PDR).

The Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) found that DME incidence over 25 years among people with type 1 DM was 29%[3]. The Diabetes Control and Complications Trial (DCCT) reported that 27% of people with T1DM had DME within 9 years of onset of diabetes[4].

DME is suspected in patients with any level of DR who present with blurred vision or metamorphopsias. A detailed history including the approximate date of onset of diabetes should be elicited.

Patients undergo a detailed biomicroscopic examination using the slit lamp biomicroscope and indirect ophthalmoscope. Historically, DME classifications were based on the ETDRS definitions of clinically significant macular edema (CSME). The specific criteria for diagnosing CSME were:

1. Retinal thickening at or within 500 µm of the center of the fovea
2. Hard exudates at or within 500 µm of the center of the fovea if adjacent to an area of retinal thickening
3. Retinal thickening of at least 1 disc area any portion of which is within 1500 µm (approximately 1 disc diameter) from the center of the fovea

Thus, CSME as defined by the ETDRS in the 1980s is a clinical diagnosis made by slit-lamp examination using a contact lens. While clinical examinations remain essential for the full evaluation of DME, Optical Coherence Tomography (OCT) is now routinely used to complement physical examination in the diagnosis of DME.

As far as treatment is concerned, at present, anti-VEGF agents, Intravitreal steroids, Laser photocoagulation are used individually or in combination in the treatment for DME.

Intravitreal triamcinolone acetonide (IVTA) has been shown to improve DME. Although much published data exists for this therapy, the optimal dose for IVTA is still under discussion.

In the current study, we used 1mg, 2mg and 4mg of IVTA injection respectively in patients with diabetic macular edema and prospectively investigate the efficacy and safety of the different doses for a period of 18 months. This will give us a better understanding of the management of the disease as to what dose of intravitreal steroid is best suited for CSME with least complications.

MATERIAL AND METHODS:

Following clinical diagnosis of a patient with diabetic macular edema, Patients were evaluated i.e. HbA1C, FBS, PPBS, Lipid Profile was done. Visual acuity, intraocular pressure, slit-lamp examination, and dilated fundoscopic examination had been performed in all patients before intravitreal injection. A fluorescein angiogram and OCT was performed at day 0. The patients were randomly distributed in groups based on their arrival and time of diagnosis they were put in group 1mg, 2mg and 4mg and the appropriate dose of IVTA administered.

The intravitreal injections were carried out in an operating room under all aseptic precautions. The injection site was usually the inferotemporal quadrant to avoid drug deposition in front of the visual axis. The stab is given 3 mm from the limbus (in aphakic and pseudophakic patients) and 3.5 mm from the limbus in phakic patients to ensure against passage of the needle through the vitreous base. The patient is usually put on a post-injection course of topical antibiotic eye drops for a week.

The patient is called for follow up after 1 day, 1 week and at day 30 and day 90 and visual acuity is measured and S/L examination is done and the IOP is measured again on day 1, day 7 day 30 and day 90. The patient is asked to follow up SOS in the OPD in case of any pain redness and discomfort. FFA and OCT was done on Day 30 and Day 90 post IVTA.

The data were analyzed using SPSS software 24 trial version. Frequency percentage, mean and standard deviation were used to summarize the data. Repeated measure ANOVA, one-way ANOVA, paired t-test and Chi-square test was used to test the level of significance ($p<0.05$).

VA improvement(Snellen's)	IVTA		
	1 mg	2 mg	4 mg
Improvement	13(52%)	14(56%)	10(40%)
No Improvement	12(48%)	11(44%)	15(60%)
Total	25	25	25

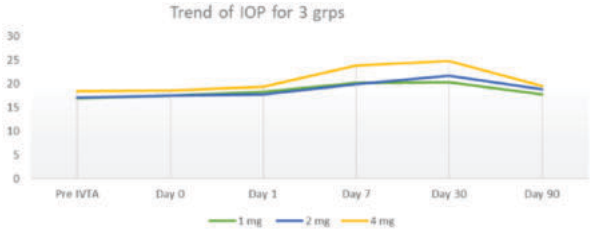
FFA outcome	IVTA		
	1mg	2mg	4mg
Diffused DME throughout	10(40%)	8(32%)	9(36%)
Reduced	15(60%)	17(68%)	16(64)
Total	25	25	25

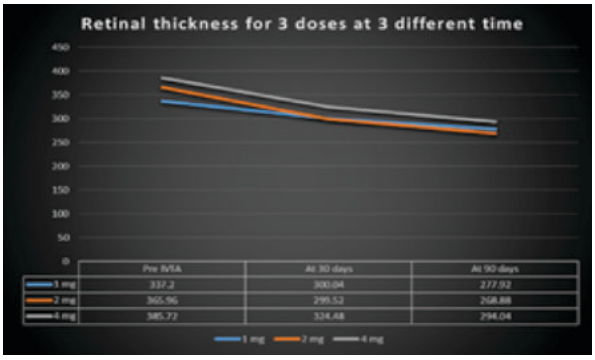
RESULTS

A total of 75 eyes of patients with DME were treated with IVTA with varying doses of 1 mg, 2 mg and 4 mg. All the 75 patients completed a 3month follow up and were all included in this study.

DISCUSSION

Our study found that overall all the three groups of IVTA showed an improvement in VA, Reduction in SCMT on OCT and Reduction in areas of leakage was seen on FFA .





Cataract Status	IVTA		
	1 mg	2 mg	4 mg
Cataract Progression	0(0%)	3(33.3%)	6(75%)
No Cataract Progression	8(100%)	6(66.7%)	2(25%)
Total	8	9	8

However it was not statistically significant but we found that that the VA improvement was similar in the 2 groups i.e. it was 52% in the 1mg group, 56% in the 2mg group and slightly lesser in the 4 mg group i.e.40%.

The reduction in area and size of leakage was almost similar in the 3 groups with a slightly better improvement in the 2 mg group, in the 1 mg group 60% of the patients showed improvement on FFA and in the 2 mg group it was 68% and in the 4mg group 64% of patients showed reduction in area of leakage.

A study done by Bakri S J,Beer P M et al showed marked improvement of macular edema on FFA after 4 mg IVTA in 21.6%, mild improvement in 52.6% and no change in 26.3%; no patient had worsening of macular edema. The triamcinolone was well tolerated, and there were no other ocular complications. This study showed similar results to our study with regards to improvement of DME on FFA[5].

There was a measurable reduction in the SCMT in the 2 mg and the 4mg group than that in the 1mg group there was a mean reduction of 59.28 micron meters in the 1mg group and 97.08 micronmeteres in the 2mg group and 91.68 micrometer in the 4 mg group.

Francois Audren, MD Amelie Lecleire, MD Ali Erginay, MD Belkacem Haouchine et all conducted a study on 4mg v/s 2mg IVTA and concluded that 4mg or 2mg Triamcinolone Acetonide for DME seem to result in similar improvement of both SCMT and VA[6].

Despite the randomization of the patients in each group we noticed that the patients who received 4mg IVTA had a lesser improvement in the VA but the improvement on FFA and OCT was significantly more compared to the 1mg group but almost similar to that of the 2 mg group.

The patients in the 4 mg group had a low VA and increased SCMT on OCT to begin with and thus despite the improvement on OCT and FFA still showed lesser improvement overall in comparison to the 2 mg group. None of the Patients in this study showed deterioration in the DME post IVTA injection irrespective of the dose of IVTA administered.

The complications such as IOP rise and Cataract progression were seen to be more significant in the 4mg group as compared to the 1 mg and 2 mg groups. The IOP rise began as early as on day 7 post IVTA and was the highest at the end of 1 month but regressed back to normal by the end of 3 months with topical antiglaucoma medications.(the mean pressures noted in the 4 mg group were 24.72 mmHg) .

Kim JE , Pollack JS, Miller DG conducted a study with 2 mg and 4 mg IVTA in DME which showed that IOP rise was more in the 4mg group than that of the 2 mg group which is similar to our study[7].

David Hauser, MD Amir Bukelmn, MD Russell Pokroy, MD Haia Katz showed that the higher dose i.e. 4mg compared to a 2mg dose had a more sustained effect on both VA and SCMT, although with a trend to more ocular hypertensive responses. Presently, they use a preservative free preparation, in doses of 2 mg[8].

The cataract progression was seen to be more in the 4 mg group than the 2 mg group and the 1 mg group showed no cataract progression till the last follow up.

Our study shows that the use of the higher 4 mg dose of IVTA, preservative free, does not have enough advantage over the lower 1 and 2 mg doses to overcome the imbalances in the 4 mg group outlined above, and to warrant the slightly higher risk of glaucoma with the 4 mg dose.

Our findings corroborate the recent study of Audren et al, who found no significant difference in VA, CMT between 2 and 4 mg doses.

On the other hand, Lam et al recently published a comparison between 4 and 8 mg doses. They showed that the higher dose had a more sustained effect on both VA and CMT, although with a trend to more ocular hypertensive responses[9].

CONCLUSION

Our study showed that the higher dose had a more effect on both FFA and SCMT, although with a trend to elicit a more ocular hypertensive response with increased cataractous changes in phakic patients, therefore we concluded that a dose of 4mg of IVTA does not appear to be more effective than 2 mg factoring in the improvement and the post IVTA complication rates. The optimal IVTA dose will become apparent with further study, with larger subject numbers and with more balanced study groups.

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