ORIGINAL Prof-1243

VISUAL ACUITY;

ASSESSMENT OF EFFICACY AND SAFETY OF DIFFERENT DOSES OF INTRAVITREAL TRIAMCINOLONE.

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ABSTRACT ... Purpose: To compare efficacy of different doses of intravitreal triamcinolone on the best corrected visual acuity and assess the safety of the drug. **Materials and methods:** The study was carried out at Al-Shifa Trust Eye hospital Rawalpindi, and Rawalpindi General Hospital Rawalpindi. 99 eyes of 99 patients with clinically significant macular edema were randomized to treatment with 2mg, 4mg, 6mg and 8mg of intravitreal triamcinolone.19 patients were lost in the follow up. Follow up of the patients was scheduled for twenty four weeks to assess the changes in the best corrected visual acuity and the side effects of the drug such as rise in intra ocular pressure between the four groups. **Results:** There was a significant improvement of best corrected visual acuity in all the four groups. The mean BCVA improvement in the 8mg was higher than the 2mg group with an improvement of 2 lines and 1 line respectively. (P=0.04). the rise in the intra ocular pressure (>21mg) occurred in 5%, 5%, 5% 40% in the 2mg, 4mg,6mg and the 8mg respectively. **Conclusions:** The higher doses of intravitreal triamcinolone may increase and prolong the visual benefits in cases of clinically significant macular oedema but the rise in intra ocular pressure remains an area of concern. More studies are required to assess the optimum dose of intravitreal triamcinolone.

INTRODUCTION

Clinically significant macular oedema remains a dark area in the ophthalmologist's treatment strategies. A number of therapies have been advanced to solve the problem like drugs and laser treatment but no modality has so far lived up to its promise. The use of intravitreal triamcinolone in the treatment of clinically significant macular oedema has had its benefits and drawbacks but its evaluation is still going on[1-4]. 4 mg intravitreal triamcinolone is currently used but with short term benefits but higher doses have also been used[5]. To have better results we have tried higher doses to have a sustained effect on the visual acuity with tolerable side effects.

MATERIALS AND METHODS

This study was conducted at Al-Shifa Trust Eye Hospital Rawalpindi and Rawalpindi General Hospital from January 2005 to December 2005. 99 patients were registered in the retina clinic and were scheduled for the follow ups in next twenty four weeks.19 patients were lost in the follow up. It was a prospective randomized study on patients attending the retina clinic. The inclusion criteria included patients with clinically significant macular oedema according to early treatment of diabetic retinopathy study[6]. Patients with previous

history of laser or surgical treatment were excluded from the study. Similarly the patients with diabetic retinopathy of more than severe non proliferative diabetic retinopathy were also omitted as the severity of the generalized retinopathy might also affect the outcome of the study.

All the patients underwent ophthalmic examination which included best corrected visual acuity on Snellen visual acuity chart, slit lamp biomicroscopy for the anterior segment examination and slit lamp biomicroscopy with contact lenses to assess the posterior segment pathology. The status of the lens opacity was graded according to the lens opacity classification system. The intra ocular pressure was measured with Goldmann applanation tonometer. 2mg, 4mg, 6mg, and 8mg of intravitreal triamcinolone was injected to the patients on random basis.

Injection procedure;
The injections were given in the retina clinic outpatient department using aseptic measures. A drop of Proparacaine was used to achieve local anesthesia. Then Povidine iodine 5% was instilled into the conjunctival sac and left for 5 minutes. After that a pledget soaked in proparacaine was applied to the site of the injection for one minute to locally anaesthetize it. This was followed by intravitreal injection of triamcinolone acetonide at a distance of 3.5 mm from the limbus at the pars Plana site using a 27 gauge needle. The preparations made for the injection ware 2mg in 0.05ml, 4mg in 0.1ml, 6mg in 0.15ml, and 8mg in 0.2ml. An examination was then made to look for any immediate complications like vitreous hemorrhage, lens damage and increase in the intra ocular pressure. If there was an increase in the intra ocular pressure affecting the central artery pulsation, then potent antiglaucoma medications were given like tablets diamox or infusion mannitol and topical medications. If the intra ocular pressure was above 40mm then anterior chamber paracentesis was also done along with the antiglaucoma medication. If there was no immediate complication then ofloxacin eye drops and timolol eye drops were prescribed for one week.

The patients were examined on day 1, and weeks 1, 4, 12 and 24 weeks with complete ophthalmic examination including best corrected visual acuity. The complications were also noted if any. Intra ocular pressures of excess of 21mm were given treatment until there pressures were less than 18mm with no traces of triamcinolone in the vitreous cavity.

RESULTS

A total of 99 eyes fulfilled the inclusion criteria and the patients were recruited in the study.19 patients failed to make in the follow up examinations during the six month period and were omitted from the study. There was no significant difference in the baseline age, sex, intra ocular pressure and the best corrected visual acuity in the 2mg, 4mg, 6mg and the 8mg groups.

Table-I. Baseline characteristics of patients

Dose of intravitreal injection	2mg	4mg	6mg	8mg	p value
Total no. of patients	20	20	20	20	20
Male; female ration	12:8	11:9	12:8	13:7	0:6
Mean (SD) age (years)	55.2(6.4)	56.4(7.7)	54.6(7.3)	59(8.2)	0.77
Mean (SD) BCVA (Snellen)	6/60 (0.31)	6/36 (0.29)	6/60 (0.28)	6/60 (0.32)	0.003
Mean (SD) intraocular pressure	14.2 (3.9)	13.7 (4.0)	15.2 (2.7)	14.5 (2.7)	0.98

Table-II. Changes in best corrected visual acuity (No. Of Snellen Letters)									
Follow up period	**2mg**	**SD**	**4mg**	**SD**	**6mg**	**SD**	**8mg**	**SD**	**p value**
BCVA improvement at 2 weeks	4.1	8.4	6.5	8.5	7.1	8.2	8.5	7.3	0.49
BCVA improvement at 4 weeks	7.5	9.2	8.5	9.7	8.9	9.7	9.2	10.5	0.44
BCVA improvement at 12 weeks	6.0	8.5	8.4	9.5	9.1	9.9	10.3	10.7	0.30
BCVA improvement at 24 weeks	2.2	9.6	4.5	8.6	8.6	9.5	10.3	10.4	0.049
No of eyes with BCVA improvement	Of > 15 letters at 6 months		1(5%)		1(5%)		4(25%)		6(33%)
No of eyes with BCVA deterioration	Of > 15 letters at 6 months		5(25%)		1(5%)		1(5%)		1(5%)

Table-III. Baseline characteristics of patients					
Dose of intravitreal injection	**2mg**	**4mg**	**6mg**	**8mg**	**p value**
Eye with maximum IOP > 21 mm (%)	1(5%)	1(5%)	1(5%)	8(40%)	0.3
Mean no. of glaucoma drugs per eye	1	1	1.8	2.2	0.10
Surgical intervention for glaucoma	0	0	0	4(20%)	-
Increase in cataract (%)	1(5%)	1(5%)	1(5%)	2(10%)	0.43
Vitreous haemorrhage	0	0	0	0	-
Vitritis	0	0	1	0	-

The best corrected visual acuity was assessed at all the follow ups. There was a maximum visual improvement of 7.5 and 8.5 letters at 4 weeks in the 2mg and the 4mg groups respectively whereas there was a maximum visual improvement of 9.1 and 10.3 letters at 12 weeks in the 6mg and 8mg group respectively. Similarly there was an improvement of 15 or more letters in 6 patients in the 8 mg group as compared to 1 in the 4 mg group. The rise in the intra ocular pressure >21mm was observed at 4 weeks in the 4mg group as compared to 2 weeks in the 8 mg group. Similarly the patients on antiglaucoma therapy were also higher in the 8 mg group as shown in table-III and a significant number (4 patients; 20%) were uncontrolled on medication and surgical intervention in the form of trabeculectomy was done. There was no significant difference in the cataract formation in all the 4 groups. Fortunately no severe complications like endophthalmitis and retinal detachment were noted.

DISCUSSION

A number of studies have been conducted so far to assess the safety and efficacy of various doses of intravitreal triamcinolone in patients diagnosed to have clinically significant macular oedema[7]. A study by Lam et al has suggested that higher doses of intravitreal triamcinolone may prolong the duration of visual benefit in diabetic clinically significant macular oedema and seemed to result in more sustained reduction of macular oedema. Although it is a suggestive of higher doses to be used but they have suggested for further studies to find the optimum dose for the treatment of clinically significant macular oedema. Spandau et al compared the effects of 2 mg, 5 mg, and 13 mg of intravitreal triamcinolone in patients with diffuse diabetic macular

oedema which revealed that by increasing the dosage of intra-vitreal triamcinolone resulted in more prolonged and more pronounced visual improvement and treatment response[8]. In our study the number of letters improved in the 8 mg group was significantly more than the lower dosage groups. Similarly the visual improvement was sustained more so in the 8 mg group as 6 of the patients still had improve visual acuity at 6 months. In contrast the 2mg and the 4 mg group the benefits of intravitreal triamcinolone was maximum at the 4 week follow-up but it eventually faded out as there was only one patient of improvement of 15 or more letters at the 6 month period.

In terms of side effects no serious complication was noted in our study like endophthalmitis and retinal detachment. The most common complication noted was raised intra ocular pressure. The proportion of eyes with raised intra ocular pressure was significantly higher in the 8 mg group as compared to the lower dosage groups. The percentage of patients with raised intra ocular pressure was lower than reported in other studies reported in a range of 16.6% to 41.2% by Ozkiris et al and Jonas et al[5, 9]. The number of patients using the antiglaucoma medication and undergoing trabeculectomies in the event of medically uncontrolled medication was also higher in the higher dosage 8 mg group. There was no significant difference in the formation of cataract formation in all the groups.

CONCLUSION

To conclude, it can be said that the higher dosage of intravitreal triamcinolone has the benefits of more increased and sustained effects on the best corrected visual acuity but at the cost of higher side effects the most common of which is the rise in the intra ocular pressure. The dosage of 6 mg was found to have beneficial and sustained effects with minimum complications in contrast to the 8 mg group which had similar benefits on visual acuity but with early and more rise in intra ocular pressure which may not be controlled on medications and result in surgical intervention. The 2mg and the 4mg groups had less side effects but did not have sustained effects on the visual acuity. Hence the 6mg is suggested for intravitreal triamcinolone injection for treatment of clinically significant macular oedema.

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