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Intravitreal triamcinolone acetonide as an additional tool in pars plana vitrectomy for proliferative diabetic retinopathy

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PURPOSE. To evaluate the safety and efficacy of intravitreal injections of crystalline triamcinolone acetonide as an adjunctive procedure in pars plana vitrectomy for proliferative diabetic retinopathy.

METHODS. This nonrandomized comparative study included 30 patients (32 eyes) who underwent standardized pars plana vitrectomy for treatment of proliferative diabetic retinopathy and who received an intravitreal injection of 25 mg triamcinolone acetonide at the end of surgery. Mean follow-up time was 5.60 ± 5.14 months. The study group was compared with a control group (32 eyes) matched with the study group for preoperative and intraoperative parameters and who underwent pars plana vitrectomy for proliferative diabetic retinopathy without intravitreal injection of triamcinolone acetonide.

RESULTS. The study group and the control group did not vary significantly in frequency of postoperative retinal detachment, re-pars plana vitrectomy, or postoperative enucleation or phthisis bulbi, or in best postoperative visual acuity, visual acuity at end of the study, or gain in visual acuity.

CONCLUSIONS. In this pilot study, the study group with pars plana vitrectomy and intravitreal triamcinolone acetonide injection compared with the nonrandomized control group without intravitreal triamcinolone acetonide injection did not show a higher than usual rate of postoperative complications. As a corollary, however, the data do not suggest the adjunct use of 25 mg intravitreal triamcinolone acetonide combined with pars plana vitrectomy as treatment of proliferative diabetic retinopathy. (Eur J Ophthalmol 2003; 13: 468-73)

KEY WORDS. Intravitreal triamcinolone acetonide, Diabetic retinopathy, Diabetic macular edema, Intraocular pressure, Steroid response

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INTRODUCTION

Intravitreal triamcinolone acetonide has increasingly been used as adjunctive treatment for intraocular neovascular, proliferative, or edematous diseases such as diffuse diabetic macular edema, neovascular glaucoma, and exudative age-related macular degeneration (1-25). In a previous small pilot study, the effect of an intravitreal injection of crystalline cortisone as adjunctive procedure in pars plana vitrectomy (PPV) for proliferative diabetic retinopathy (PDR) was examined (11). The pilot study concluded that intravit-

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TABLE I - PREOPERATIVE AND INTRAOPERATIVE CLINICAL DATA OF THE STUDY GROUP UNDERGOING PARS PLANA VITRECTOMY AND INTRAVITREAL INJECTION OF CRYSTALLINE TRIAMCINOLONE ACETONIDE AND THE CONTROL CROUP UNDERGOING PARS PLANA VITRECTOMY WITHOUT INTRAVITREAL INJECTION OF TRIAMCINOLONE ACETONIDE

	Study group	**Control group**
No. eyes	32	32
Age, y, mean ± SD	62.69 ± 9.28	59.29 ± 16.32
Median (range)	64.23 (27.96-80.66)	61.01 (26.56-85.60)
Females/males	19/11	17/15
Right eye/left eye	17/15	13/19
Refractive error, D, mean ± SD	0.27 ± 1.52	-0.03 ± 0.75
Median (range)	0.00 (3.25 to + 4.63)	0.00 (-2.50 to +2.13)
Preoperative visual acuity, mean ± SD	0.03 ± 0.05	0.03 ± 0.05
Median (range)	0.03 (Light perception-0.20)	0.01 (Light perception-0.20)
Preoperative intraocular pressure, mmHg, mean ± SD	16.3 ± 4.6	14.22 ± 7.16
Median (range)	16 (6-28)	14 (6-48)
Iris neovascularization, n (%)	9 (28.1)	5 (15.6)
Previous vitreoretinal procedures, n (%)	8 (25)	1 (3.1)
Pseudophakia, n (%)	11 (34.4)	12 (37.5)
Membrane peeling, n (%)	25 (78.1)	27 (84.4)
Retinal endolaser coagulation, n (%)	28 (87.5)	14 (43.8)
Number of endolaser coagulation spots, mean ± SD	2423 ± 792	1650 ± 806
Median (range)	2400 (1000-3920)	1748 (173-2857)
Silicone oil endotamponade, n (%)	15 (46.9)	14 (43.8)
Intraoperative use of perfluorocarbon liquids, n (%)	5 (15.6)	5 (15.6)
Peripheral retinotomies/retinal defects, n (%)	5 (18.7)	7 (21.9)
Paracentral retinotomy/retinal defects, n (%)	1 (3.6)	0
Peripheral cryocoagulation, n (%)	8 (25)	15 (46.9)
Extensive peripheral cryocoagulation, n (%)	2 (6.2)	2 (6.2)
Cataract surgery, n (%)	10 (31.3)	6 (18.8)
Removal of cyclitic membranes, n (%)	2 (6.3)	0

real injection of crystalline cortisone may not be toxic to intraocular structures, reduces postoperative intraocular inflammation, and may be a potentially useful additional tool in the treatment of PDR.

In view of the lack of long-term experience with intravitreal triamcinolone acetonide injections, and considering that the mean follow-up period in the pilot study was only 1.4 months (median 1 month), we performed a follow-up study on the patients included in the original investigation, extending their follow-up period, including several new patients, and including a control group to compare the results of the patients in the study group with the results of the patients in the control group.

PATIENTS AND METHODS

The study included 32 eyes of 30 patients who underwent PPV for treatment of PDR, received an intravitreal injection of crystalline triamcinolone acetonide at the end of surgery, and were operated on by the same surgeon. All patients included in the study showed persistent vitreous hemorrhage due to diabetic retinopathy for at least 3 months prior to surgery, and all eyes exhibited central retinal traction detachment with involvement of the macula. The study group was prospectively formed and treated. Mean age was 62.69 ± 9.28 years, preoperative visual acuity (VA) measured 0.03 ± 0.05, preoperative intraocular pressure was 16.3

TABLE II - POSTOPERATIVE DATA OF THE STUDY GROUP UNDERGOING PARS PLANA VITRECTOMY AND INTRAVITREAL INJECTION OF CRYSTALLINE TRIAMCINOLONE ACETONIDE AND THE CONTROL GROUP UNDERGOING PARS PLANA VITRECTOMY WITHOUT INTRAVITREAL INJECTION OF TRIAMCINOLONE ACETONIDE

	Study group	**Control group**
No. eyes	32	32
Follow-up period, mo, mean ± SD	5.60 ± 5.14	10.53 ± 11.64
Median (range)	4.01 (0.20–16.57)	5.48 (0.20–46.30)
Best postoperative visual acuity, mean ± SD	0.08 ± 0.08	0.08 ± 0.11
Median (range)	0.05 (Light perception–0.30)	0.05 (Light perception–0.50)
Last visual acuity, mean ± SD	0.06 ± 0.08	0.05 ± 0.09
Median (range)	0.01 (No light perception–0.30)	0.01 (No light perception–0.40)
Change in best visual acuity, mean ± SD	+0.05 ± 0.10	+0.05 ± 0.11
Median (range)	0.02 (-0.20 to +0.30)	0.01 (-0.10 to +0.40)
Change in visual acuity at study end, mean ± SD	+0.03 ± 0.09	+0.03 ± 0.08
Median (range)	0.02 (-0.20 to +0.30)	0.001 (-0.10 to +0.30)
IOP 1 week postoperatively, mm Hg, mean ± SD	14.75 ± 4.24	14.41 ± 4.74
Median (range)	16 (7–23)	15 (3–24)
Intraocular pressure at end of the study, mean ± SD	14.34 ± 6.58	12.61 ± 5.65
Median (range)	14.5 (2–31)	14 (0–21)
Retinal detachment, n (%)	6 (18.8)	4 (12.5)
Re-pars plana vitrectomy, n (%)	4 (12.5)	2 (6.25)
Enucleation or phthisis bulbi, n (%)	0	2 (6.25)

± 4.6 mmHg (Tab. I). Iris neovascularization was present in 9 (28.1%) eyes: 2 (6.3%) showed a slight degree of iris neovascularization, 2 (6.3%) exhibited a moderate degree of rubeosis iridis, 2 (6.3%) had developed a medium to advanced degree of iris neovascularization, and 2 (6.3%) showed a marked degree of rubeosis iridis. A total of 8 (25%) eyes had previously undergone PPV for PDR. A total of 11 (34.4%) eyes were pseudophakic prior to inclusion into the study.

The standardized technique of PPV consisted of performing three pars plana sclerotomies and removing the vitreous including the posterior vitreous surface. Depending on the clinical situation, additional procedures were performed, such as peeling of epiretinal membranes, retinal endolaser coagulation, peripheral retinal cryocoagulation, use of silicone oil endotamponade (viscosity 5000 centistoke), temporary application of perfluorocarbon liquids, and performing peripheral or paracentral relaxing retinotomies (Tab. I). In 2 (6.3%) eyes with marked iris neovascularization, cyclitic membranes expanding from the ciliary body on one side of the globe to the ciliary body on the other side of the globe had to be removed during surgery. At the end of surgery, 25 mg of crystalline triamcinolone acetonide was injected through the closed sclerotomies into the vitreous cavity in the direction of the peripheral retina at the 6 o'clock position. Care was taken that triamcinolone acetonide was injected free of the vehicle, which may be toxic to the intraocular tissues. After closure of the conjunctiva, gentamicin was injected subconjunctivally. At the end of surgery, the patients were asked to sit up and to keep an upright position for at least 2 hours after surgery to prevent the cortisone crystals from falling onto the macular region. PPV was carried out with general anesthesia in 6 (18.8%) eyes. For the remaining 25 (78.1%) eyes, surgery was performed with local anesthesia, using the retrobulbar catheter technique (26). Mean follow-up time was 5.60 ± 5.14 months (Tab. II).

The study group was compared with a control group consisting of 32 patients (32 eyes) with PDR who underwent PPV in a similar manner as the patients in the study group and who were operated on by the same surgeon who used the same technique and the

same surgical instruments. All eyes showed vitreous hemorrhage and exhibited central retinal traction detachment with involvement of the macula. The patients of the control group, which was formed retrospectively, were matched with the patients of the study group for preoperative VA, preoperative intraocular pressure, preoperative refractive error, duration of vitreous hemorrhage prior to inclusion in the study, age, sex, prevalence of pseudophakia, use of silicone oil endotamponade, frequency of intraoperative retinal breaks, and frequency of intraoperative transscleral retinal cryocoagulation (Tab. I). The difference between the study group and the control group was that the patients in the control group did not receive an intravitreal injection of triamcinolone acetonide.

RESULTS

In the study group, best postoperative VA measured 0.08 ± 0.08 (Tab. II). At the end of the follow-up period, VA was 0.06 ± 0.08. Change in best VA (difference of best postoperative VA minus preoperative VA) was on average +0.05 ± 0.10. In 5 (15.6%) eyes, best postoperative VA was worse than the preoperative VA measurements. In 19 (59.4%) eyes, postoperative VA was better than the preoperatively determined measurements. In the remaining 8 (25%) eyes, preoperative and postoperative VA measurements did not differ. Mean change in VA measured at study end versus the preoperative determinations was +0.03 ± 0.09 (Tab. II). The last postoperative VA measurements were worse than the preoperative measurements in 7 (21.9%) eyes, and they were better in 13 (40.6%) eyes. Postoperative VA was statistically independent of preoperative VA ($p=0.70$), development of peripheral retinal breaks ($p=0.46$), number of retinal endolaser coagulation spots ($p=0.31$), and number of cryocoagulation spots ($p=0.33$).

One week after surgery, intraocular pressure measured 14.75 ± 4.24 mmHg (range, 7 to 23 mm Hg) (Tab. II). It was higher than 21 mmHg in 2 (6.2%) eyes, with measurements of 22 mm Hg and 23 mmHg.

A detachment of the retina was detected in 6 (18.8%) eyes at the end of the follow-up period. A re-PPV was performed in 4 (12.5%) eyes due to a retinal detachment (n=3) or recurrence of vitreous hemorrhage in an eye without silicone oil endotamponade (n=1). Three of the six eyes with a retinal detachment did not undergo any further vitreoretinal surgery. Development of retinal detachment was significantly ($p=0.04$) associated with the presence of intraoperative retinal breaks in the paracentral region. It was statistically independent of the occurrence of peripheral retinal breaks during surgery ($p=0.32$), number of endolaser coagulation spots ($p=0.36$), and number of retinal cryocoagulation spots ($p=0.85$).

Three eyes became phthisical. One of them had presented preoperatively with a VA of light perception. During surgery, a peripheral retinal defect occurred, and 3150 endolaser coagulation spots were set. After surgery, VA steadily increased from light perception to a value of 0.10 with an intraocular pressure of 10 mm Hg at 3.5 months after surgery. Four weeks later, intraocular pressure had dropped to 2 mmHg, vision was gone, and the eye became phthisical. The second eye becoming phthisical had showed a pronounced cyclitic membrane preoperatively and had a preoperative VA of light perception. The third eye had developed secondary angle-closure glaucoma due to marked iris neovascularization preoperatively.

Comparing the study group with the control group, best postoperative VA, VA at end of the study, gain in VA with respect to best postoperative VA, and gain in VA with respect to VA at the end of the study did not vary significantly ($p>0.30$) between the two groups (Tab. II). Correspondingly, the frequencies of postoperative retinal detachments, re-PPV, and enucleation or phthisis bulbi did not differ significantly ($p>0.30$) between the two groups (Tab. II). Intraocular pressure did not vary significantly between the two groups 1 week after surgery ($p=0.26$). Intraocular pressure was significantly higher ($p<0.05$) in the study group than in the control group at the end of the follow-up period.

After 2 to 4 months, all triamcinolone acetonide crystals were resolved. No cases of infectious endophthalmitis occurred postoperatively.

DISCUSSION

In the present study, the effect of an intravitreal injection of triamcinolone acetonide on the outcome of PPV as treatment of PDR was investigated. The patients of the study group receiving the intravitreal injection of triamcinolone acetonide and the patients of

the control group without intravitreal triamcinolone acetonide injection did not differ significantly (p>0.30) in frequency of postoperative retinal detachments, re-PPV, or enucleation or phthisis bulbi (Tab. II). In agreement with these findings, best postoperative VA, VA at the end of the study, gain in VA with respect to the best postoperative VA, and gain in VA with respect to the VA at the end of the study did not differ significantly (p>0.30) between the two groups (Tab. II). Regarding the present study as a phase I study, one may infer that the intravitreal injection of triamcinolone acetonide was not associated with a higher than expected frequency of postoperative complications. Similarly, however, one may also infer that the use of intravitreal triamcinolone acetonide in combination with PPV did not improve the final visual and anatomic outcome. Intravitreal triamcinolone acetonide appears not to be helpful when used in combination with PPV.

Direct toxic effects of triamcinolone acetonide on the intraocular tissues in the eyes with the retina postoperatively attached were not observed in the present study. This agrees with other studies in which the same dose of triamcinolone acetonide was injected for various reasons (10-13, 19-21, 23). An elevation of intraocular pressure was not a major problem in the postoperative period in the present study. A pressure rise above 21 mm Hg was observed in 2 (6.3%) patients, and in both patients could be normalized by topical antiglaucomatous treatment until the triamcinolone acetonide crystals disappeared. Interestingly, fewer patients in the present study developed secondary ocular hypertension after intravitreal injection of 25 mg triamcinolone acetonide than did patients who received the same injection as treatment of exudative age-related macular degeneration (20, 24, 25).

There are limitations of the study. It is not a randomized prospective investigation in which the patients were randomly distributed into the study group and the control group. The control group and the study group, however, were matched for preoperative data such as VA, number of retinal operations prior to inclusion in the study, and lens status, as well as intraoperative parameters such as frequency of silicone oil endotamponade, endolaser coagulation, and occurrence of intraoperative retinotomies or iatrogenic retinal breaks. Additionally, all patients in both groups were operated on by the same surgeon, who used the same instruments throughout the study. This may have reduced the influence of external factors such as experience and surgical skills of the surgeon. Another limitation of the study is that the degree of intraocular inflammation was not quantified, such as by laser tyndallometry.

In conclusion, the results of the present phase I study suggest that intravitreal injection of triamcinolone acetonide was not associated with a higher than expected frequency of postoperative complications in eyes undergoing PPV for PDR. As a corollary, however, and in contrast to the theoretical advantages of the antiphlogistic and antiangiogenic effects of triamcinolone acetonide, the data do not strongly suggest the adjunct use of intravitreal triamcinolone acetonide with PPV as treatment of PDR unless a therapeutic benefit of intravitreal triamcinolone acetonide can be proven in prospective randomized studies.

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