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Intravitreal triamcinolone for the treatment of refractory macular edema in idiopathic intermediate or posterior uveitis

B.F.T. HOGEWIND, C. ZIJLSTRA, B.J. KLEVERING, C.B. HOYNG

UMC St Radboud, Department of Ophthalmology, Nijmegen - The Netherlands

PURPOSE. *Cystoid macular edema (CME) is the most significant cause of visual loss associated with idiopathic uveitis. The authors report on the use of intravitreal triamcinolone acetonide (IVTA) in a group of patients with macular edema due to idiopathic intermediate and posterior uveitis.*

METHODS. *Retrospective, noncomparative, interventional case series. Thirty-three eyes were included with uveitic CME that was refractory to topical steroids, oral prednisone, or a combination thereof. Previous steroid treatment did not result in elevated intraocular pressure (IOP). The eyes received an intravitreal injection with 10 mg triamcinolone acetonide, after best-corrected visual acuity (BCVA) and fluorescein angiography (FA) were assessed. Ophthalmologic examination including FA was regularly performed during a 1-year follow-up period.*

RESULTS. *Within 12 weeks after injection of IVTA, 50% of the eyes responded with an improvement in vision of more than two lines and 30% of the eyes reached an IOP of ≥21 mmHg ($p<0.01$). All eyes with an elevated IOP responded well on topical antiglaucoma medication. After 12 months follow-up 40% of the eyes responded with an improvement in vision of more than two lines and 28% of the affected eyes underwent phacoemulsification during the follow-up. No other complications occurred within a year after the treatment.*

CONCLUSIONS. *In macular edema due to idiopathic intermediate or posterior uveitis IVTA improves the visual acuity within the first 3 months. However, thereafter the visual acuity decreases again. Cataract and elevated IOP are common side effects. (Eur J Ophthalmol 2008; 18: 429-34)*

KEY WORDS. *Glucocorticoids/therapeutic use, Macular edema, Cystoid/drug therapy, Triamcinolone acetonide/therapeutic use, Uveitis/drug therapy, Vitreous body*

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INTRODUCTION

Intermediate uveitis is characterized by inflammation of especially the anterior part of the vitreous body, the ciliary body, and the pars plana. Posterior uveitis is characterized by vitritis, eventually with vasculitis. Intermediate and posterior uveitis are both intraocular inflammations that can have a wide range of underlying diseases. However, in a significant amount (30–60%) of the patients, no cause for the inflammation can be assessed (1, 2). Cystoid macular edema (CME) is the most significant cause (41%) of visual impairment associated with idiopathic uveitis (3).

CME is usually treated by topical, periocular, or systemic steroids. Topical and periocular steroids, however, are often not sufficiently effective in reducing the cystoid macular edema. Systemically administered corticosteroids, on

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the other hand, can often effectively control the intraocular inflammation that causes CME, but can also induce major side effects (such as immunosuppression and Cushing syndrome). Sometimes CME persists even after inflammation is controlled (4).

Jaffe et al reported on a new and promising technique of corticosteroid deliverance into the eye: the use of fluocinolone acetonide intravitreal implants. Little is known so far on its results and side effects (5, 6). Cordero Coma et al published on the effect of the antivascular endothelial growth factor bevacizumab for uveitic macular edema (7).

Successful use of intravitreal triamcinolone acetonide (IVTA) has been reported as a potentially effective local treatment in therapy-resistant eyes with chronic uveitis (8-14). Reported complications of IVTA are secondary ocular hypertension in about 40% of the eyes injected, medically uncontrollable high intraocular pressure (IOP) leading to antiglaucomatous surgery (in about 1–2% of the eyes) (15), posterior subcapsular cataract and nuclear cataract leading to cataract surgery (in about 15–20% of elderly patients within 1 year after injection), retinal detachment, vitreous hemorrhage, postoperative infectious endophthalmitis (with a rate of about 1:1,000), noninfectious endophthalmitis, and pseudoendophthalmitis (16).

So far, two studies report on the use of IVTA for macular edema due to idiopathic intermediate or posterior uveitis in 3 and 1 patients (17, 18). The main purpose of this study was to evaluate the effect of IVTA on macular edema in idiopathic intermediate and posterior uveitis. We studied this treatment in 33 eyes out of a cohort of 23 patients for a follow-up period of 12 months.

MATERIALS AND METHODS

The retrospective, noncomparative interventional case series study was done in accordance with the principles of the Declaration of Helsinki. From 2002 through 2005 we included subjects with macular edema due to either intermediate or idiopathic posterior uveitis who had had a relapse of progressive loss of visual acuity after topical steroids, oral prednisone, or a combination thereof. The patients were fully informed about the abovementioned complications of intraocular triamcinolone.

We recorded the ophthalmic and general medical history and evaluated the best-corrected Snellen visual acuity (BCVA). Clinical examination included slit-lamp inspection and characterization of the anterior chamber, the lens, and the vitreous, IOP measurement by Goldmann applanation tonometry, and fundus examination. All study participants underwent fluorescein angiography. Common causes for uveitis were excluded by a complete general physical examination, laboratory examination of venous blood sample (including angiotensin-converting enzyme, antinuclear antibodies, antineutrophil cytoplasmic antibodies, Lues serology, Borrelia serology, and human leukocyte antigen B27 typing), urine examination, and X-thorax.

In all patients included in the study group, crystalline triamcinolone was injected intravitreally using the operating microscope. The technique of injection was standardized: the crystalline cortisone was prepared by aspirating the whole volume of a 1-mL bottle containing 40 mg of triamcinolone acetonide (Kenakort-A 40©) into a tuberculin syringe of 1 mL volume. The syringe was vertically placed on the operating table for at least 15 minutes. The crystals sedimented into the lower fifth of the syringe. The upper 0.8 mL of the syringe, containing the vehicle, was removed. The tuberculin syringe was filled with Ringer's solution, vertically placed for 5 minutes, and again the upper 0.8 mL were removed with the cortisone crystals left behind in the lower 0.2 mL. This procedure was repeated three times. Finally, the remaining 0.2 mL contained 20 mg of triamcinolone acetonide. We injected 0.1 mL of the fluid, which contained about 10 mg of triamcinolone, 4 mm (or 3.5 mm in pseudophakic eyes) posterior to the inferotemporal limbus with a 27 Gauge needle.

The follow-up period was 12 months. FA was performed after 1, 3, 6, and 12 months and compared with the baseline pictures. The changes in edema were scored independently by the authors as no change, reduction of CME, stable CME, or increase of CME. Ophthalmologic examination was performed after 1 week and after 1, 3, 6, 9, and 12 months. If IOP exceeded 25 mmHg, topical antiglaucoma therapy was started, using topical ß-blockers (timolol 0.5%) and topical carbonic anhydrase inhibitors (brinzolamide 1%), and the patient was re-examined within a month. When needed, a combination of topical drugs was prescribed. Repeat injections of IVTA were offered if the initial IVTA injection had resulted in a reduction of macular edema combined with an improvement of visual acuity followed by reduction in visual acuity with recurrence of macular edema.

Statistical analysis was performed using SPSS 12.0.1 software for Windows (SPSS Inc., Chicago, IL, USA). Intraindividual visual acuity and IOP changes during treat-

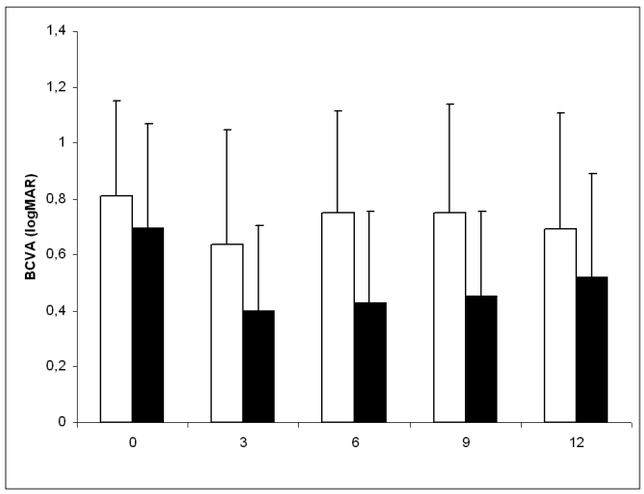

Fig. 1 - *Best-corrected visual acuity (BCVA in logMAR) of patients with uveitis prior to intravitreal triamcinolone acetonide (IVTA) treatment and at 3, 6, 9, and 12 months postoperatively. Patients are depicted with posterior uveitis (white) and intermediate uveitis (black). No significant differences were found.*

ment were put through the paired *t*-test for groups, as well as differences in gender, period of time of macular edema prior to treatment, and follow-up time after treatment. A p value <0.05 was considered to be statistically significant.

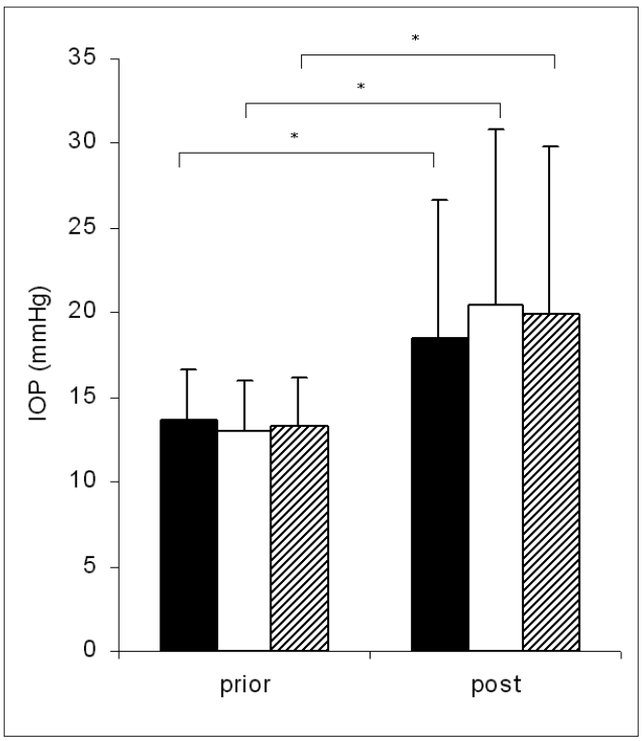

Fig. 2 - *Intraocular pressure (IOP, mmHg) of patients with uveitis prior to intravitreal triamcinolone acetonide (IVTA) treatment and the highest IOP during 3 months follow-up (p<0.01). Patients are depicted with posterior uveitis (white), intermediate uveitis (black), and posterior and intermediate together (shaded). The significant differences (p<0.05) are marked with an asterisk.*

RESULTS

From 2002 through 2005, IVTA was offered to subjects with macular edema due to therapy-resistant idiopathic intermediate or posterior uveitis and the patient records were included in the study database. All patients who were included received the treatment. Forty IVTA injections were administered in 33 eyes of 23 patients with uveitis-related macular edema. The patient group consisted of 16 female patients and 7 male patients. The mean age of the patients was 54.7 years (SD 13.0). Reasons for intravitreal injection of triamcinolone acetonide were progressive decrease of visual acuity and increase of uveitis-related macular edema despite earlier treatments. None of the patients had had elevated IOP during previous received steroid treatment. The patients were almost evenly divided between intermediate (21 eyes of 12 patients) and posterior uveitis (19 eyes of 10 patients). Mean duration of CME before TAC injection was 28.9 months (SD 28.9) in patients with intermediate uveitis, and 18.2 months (SD 14.0) in patients with posterior uveitis (p=0.01). There were no significant age and gender differences between the groups.

Repeat injections of IVTA were offered if the initial IVTA injection had resulted in a reduction of macular edema combined with an improvement of visual acuity followed by reduction in visual acuity with recurrence of macular edema. Two patients with posterior uveitis and three patients with intermediate uveitis received two injections in one eye.

Mean follow-up time was 10.6 months (SD 2.9) in the patient group with intermediate uveitis, and 11.2 months (SD 1.7) in the patient group with posterior uveitis (p=0.07).

The BCVA after IVTA increased at 3 months in both groups: 11 eyes (52%) with intermediate uveitis and 9 eyes (50%) with posterior uveitis responded with an improvement in vision of more than two lines. Twelve

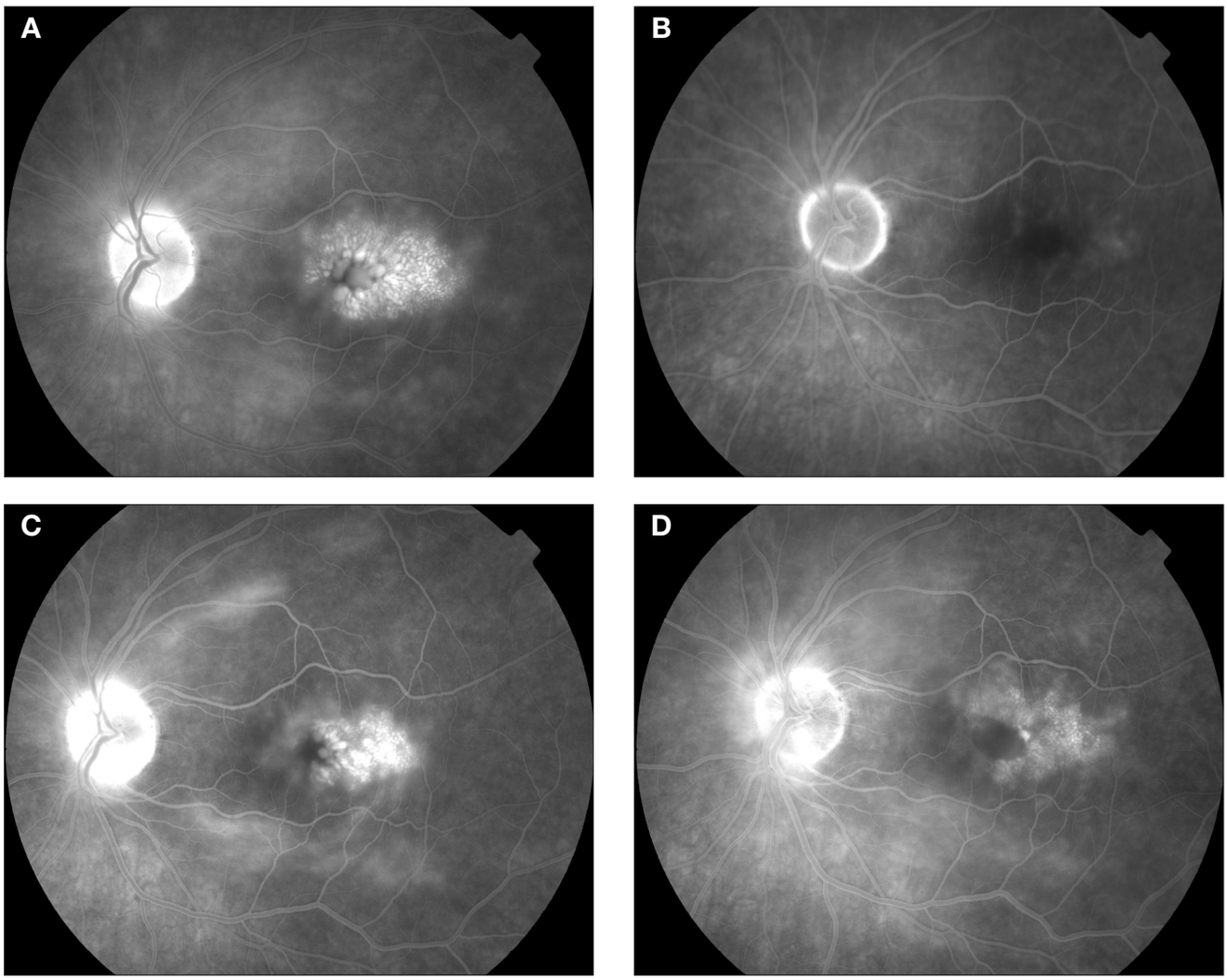

Fig. 3 - *The course of the cystoid macular edema (CME) after intravitreal triamcinolone acetonide (IVTA) treatment as followed by fluorescein angiography (FA) of one of the patients with idiopathic posterior uveitis (a 58-year-old woman).* **(A)** *The CME is depicted prior to IVTA treatment.* **(B-D)** *The same macula is depicted 3, 6, and 12 months after treatment with IVTA. The best-corrected visual acuity corresponding to the FAs is 0.4, 0.2, 0.2, and 0.3 logMAR, respectively.*

months after IVTA 10 eyes (48%) with intermediate uveitis and 6 eyes (32%) with posterior uveitis responded with an improvement in vision of more than two lines. No significant differences were found ($p>0.05$) (Fig. 1).

The mean preoperative IOP was 13.0 mmHg (SD) and 13.7 mmHg (SD) for intermediate and posterior uveitis ($p=0.99$). Within 12 weeks after injection of intravitreal TA, 12 eyes (5 posterior uveitis patients and 7 intermediate uveitis patients) reached an IOP of more than 21 mmHg (30%, $p<0.05$) (Fig. 2). None of the eyes exceeded an IOP of 40 mmHg for longer than 1 month or needed filtering surgery.

The course of the edema as followed by FA is depicted in Figure 3 and Table I.

Cataract surgery was performed in 12 (36%) of 33 treated eyes of patients who completed 12 months of follow-up (no increase of macular edema was assessed postoperatively in any of the 12 cases).

No retinal detachment, vitreous hemorrhage, or postoperative (non)infectious endophthalmitis were found.

TABLE I - FLUORESCEIN ANGIOGRAPHY (FA) OF CYSTOID MACULAR EDEMA (CME) DUE TO UVEITIS 3, 6, AND 9 MONTHS AFTER TREATMENT WITH INTRAVITREAL TRIAMCINOLONE (IVTA)

CME	3 mo follow-up		6 mo follow-up		12 mo follow-up	
	Intermediate	Posterior	Intermediate	Posterior	Intermediate	Posterior
None	7	2	6	4	4	4
Reduction	11	13	9	7	5	3
Stable	2	2	4	7	4	4
Increase	1	0	1	1	5	6
Not examined	0	2	1	0	0	0
Dropout	0	0	0	0	3	2

The FA is compared with baseline pictures of the patients with uveitis (21 intermediate and 19 posterior uveitis). The number of patients with a specific amount of CME (none, reduction, stable, or increase) is depicted. Patients who refrained from optical examination during the follow-up are classified as not examined, and patients who received a second IVTA injection are classified as dropout

DISCUSSION

In 30–60% of patients with uveitis worldwide no causative diagnosis can be established despite appropriate investigation (2). If the visual acuity is decreased because of CME that does not respond to topical or systemic therapy, IVTA may be considered (8, 9, 12, 16, 17). In uveitic edema in general IVTA is described to bring about a quick but temporary improvement in vision (4). The most common side effects are high IOP (15) and posterior subcapsular cataract (16).

So far, little has been reported on the use of IVTA for macular edema due to idiopathic intermediate or posterior uveitis.

In this study 40 10 mg IVTA injections were administered for CME secondary to uveitis, which resulted in an improvement of BCVA between 3 and 6 months. At 12 months follow-up this improvement decreased again. Galor et al present similar results in a retrospective observational case series with 4 mg IVTA treatment of 45 uveitic eyes (19).

Within 12 weeks after injection of IVTA, 30% of the eyes reached an IOP of more than 21 mmHg, which could be treated with topical antiglaucoma drugs. In the study of Galor et al, 13.3% of injected eyes needed glaucoma surgery (19). Twenty-eight percent of patients underwent an uncomplicated phacoemulsification of the affected eye during the follow-up. Although uveitis itself also causes cataract, the fact that the cataract in these cases all occurred in the injected eyes implies that these are secondary cataracts due to the IVTA. No severe complications occurred within a year after the treatment.

A major disadvantage of the study, and all other studies in this field, is the fact that there was no control group.

We propose that IVTA is a safe therapy for macular edema due to idiopathic intermediate or posterior uveitis and improves visual acuity. However, the duration of the effect is limited. The different side effects of the therapy, especially elevation of IOP and cataract, are both common and respond well to treatment.

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Reprint requests:
Barend F.T. Hogewind, MD
UMC St Radboud West
Philips van Leydenlaan 15
6500HB Nijmegen, The Netherlands
b.hogewind@ohk.umcn.nl

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