SCIENTIFIC CORRESPONDENCE

Intravitreal triamcinolone in subfoveal recurrence of choroidal neovascularisation after laser treatment in macular degeneration

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Background: Laser treatment of extrafoveal well delineated choroidal neovascularisation in exudative age related macular degeneration has a high rate of failure with subsequent severe vision loss from subfoveal involvement. Laser treatment may limit scotoma size, but is unpalatable because of early persistent vision loss. Intravitreal triamacinolone injection may be an acceptable alternative therapy in such disparate cases.
Methods: 14 consecutive patients with recurrent neovascularisation were treated with a single 4.0 mg injection of triamacinolone and followed for up to 1 year. Visual results were compared with published data from the Macular Photocoagulation Study of recurrent neovascularisation.
Results: Mean visual acuity remained stable at about 20/200 throughout the study period in the treated patients. This is comparable to the outcomes in the Macular Photocoagulation Study for laser retreated patients, and better than the observation group.
Conclusions: Intravitreal triamcinolone may be an acceptable treatment of subfoveal recurrent neovascularisation while avoiding early persistent vision loss from laser retreatment.

At this time, laser photocoagulation is the only treatment that has proved to be effective for extrafoveal well delineated (type 1) choroidal neovascular membranes (CNVM).[1 2] Unfortunately, recurrence of the CNVM is common and recurrent subfoveal CNVM results in significant deterioration of acuity.[1] Repeat laser treatment of the subfoveal lesion has been associated with somewhat better visual outcome.[2]

Triamcinolone acetonide (TAAC) is a relatively insoluble steroid that has been used for decades in the treatment of ocular inflammation by peribulbar or sub-Tenon's injection. The toxicity and pharmacokinetics of intravitreal TAAC injection have been investigated in animal models. The duration of visible intravitreal crystalline TAAC is about 2 months, presumably giving an extended period of time for its actions to occur in tissues adjacent to the vitreous cavity.[3]

The mechanism by which steroids inhibit fibrovascular proliferation is potentially multifactorial. Corticosteroids are known to inhibit cell mediated inflammation as well as leucocyte adhesion and extravasation, each of which are observed factors in the pathogenesis of age related macular degeneration (AMD).[4] TAAC also affects vascular endothelial cell extracellular matrix turnover[5] and retinal pigment epithelium responses which may include increased blood-retinal barrier function and downregulation of the VEGF gene.[4] All processes are possible contributors to the neovascular process involved in exudative macular degeneration (EAMD) that could be inhibited by corticosteroid use.

Penfold *et al*[6] and Challa *et al*[7] have reported on a small uncontrolled clinical trial of TAAC in previously untreated EAMD. Intravitreal TAAC injection appeared to be well tolerated, with a favourable effect on the course of the disease over an 18 month period. We conducted a small, randomised trial of intravitreal TAAC injection as primary treatment in subfoveal CNVM[8] and also obtained favourable short term visual acuity results.

In this uncontrolled consecutive case series, patients with subfoveal recurrent CNVM after laser photocoagulation for EAMD were treated with intravitreal TAAC and followed for 1 year after treatment.

METHODS

A consecutive series of 14 eyes of 13 patients were treated with intravitreal TAAC injection after subfoveal recurrence of neovascularisation after laser treatment of extrafoveal CNVM in EAMD. All eyes had one or more photocoagulation sessions with krypton laser treatment in Macular Photocoagulation Study fashion for well delineated extrafoveal CNVM,[1 2] as determined by clinical examination and fluorescein angiography. Failure of laser treatment or recurrence after initial improvement was heralded in each case by increased subretinal fluid, blood and/or fibrosis, as well as typical evidence by fluorescein angiography. Patients were offered TAAC injection when recurrences were subfoveal and further laser was refused.

After informed consent, patients were given several drops of topical oxybuprocaine (proparacaine), followed by a drop of 5% betadine. The patient was slightly reclined in the examining chair and asked to gaze upward. Stabilising the lids with the non-dominant hand, the injection was performed using a 27 gauge needle on a 1 ml syringe. The injection consisted of 0.1 ml of a commercially available suspension of triamcinolone acetonide (Kenalog 40 mg/ml, Apothecon) and the needle penetrated through the 6-00 pars plana (approximately 4 mm from the limbus). The needle was introduced only 2–3 mm into the eye in an effort to keep the suspension in the inferior vitreous region, out of the visual axis. After slow injection (3 or 4 seconds), the fundus was then visualised by slit lamp biomicroscopy until retinal circulation was re-established. Patients were asked to return for weekly assessment of intraocular pressure for at least the first 4 weeks after injection and were treated with topical antiglaucoma medications if the IOP became elevated over 25 mm Hg.

Visual acuity was measured, best corrected, on a front lit Bailey-Lovie chart at 10 feet at 3 month intervals. The presence of cataract was noted by slit lamp examination and graded according to the Age-Related Eye Disease Study protocol. A progression of one unit of the lens grade for nuclear sclerosis, cortical cataract, or posterior subcapsular change was considered significant. All but three eyes were followed for 1 year

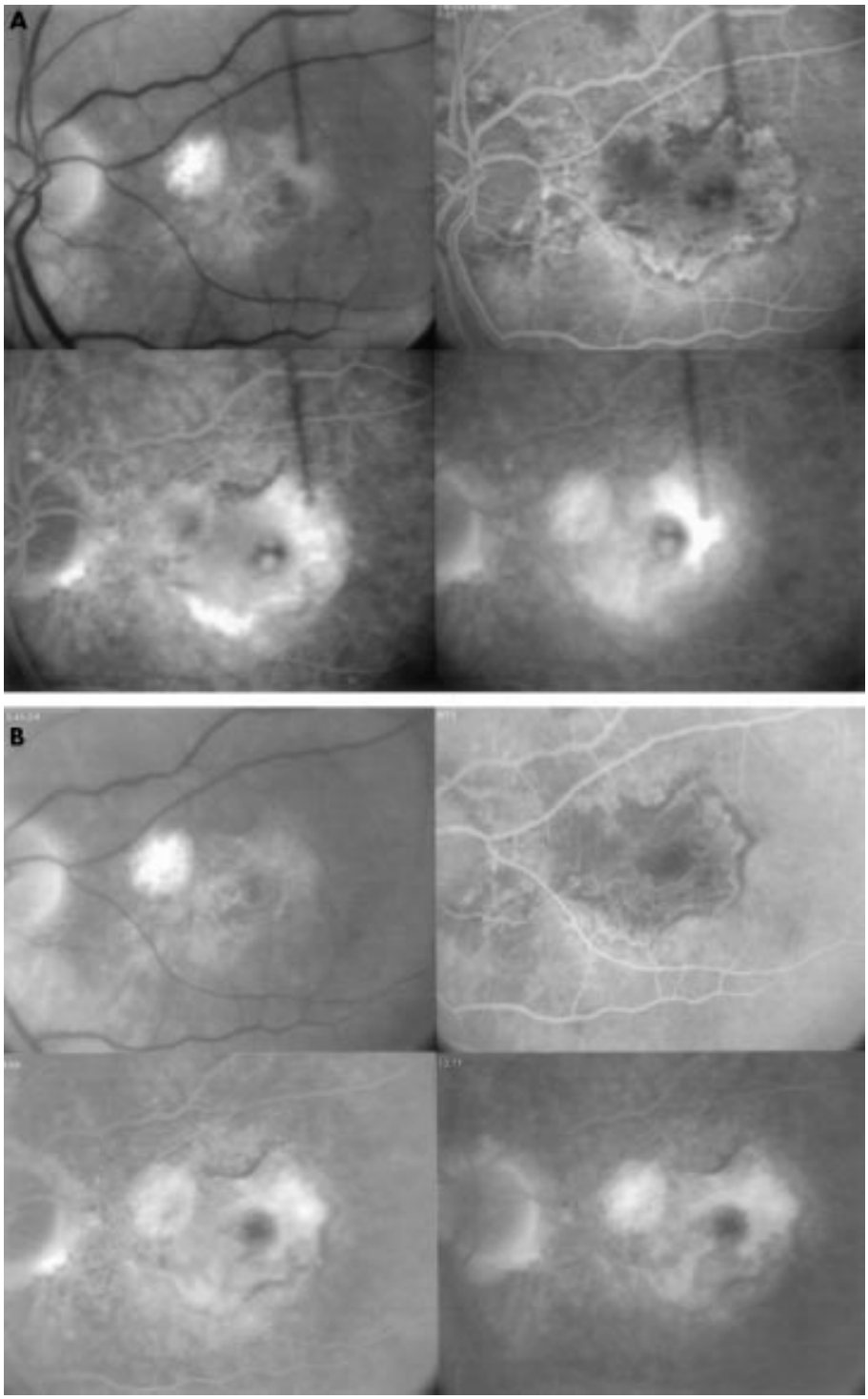

Figure 1 (A) Baseline photography and angiography of patient 1. Shown are the black and white fundus image, and early, mid, and late phases of the fluorescein angiogram. The laser scar is superonasal to the fovea and a large distinct neovascular membrane has extended through the foveal region. Visual acuity is 10/200. (B) At 6 months post-treatment with intravitreal triamcinolone, vision remains 10/200 and the photographic and angiographic images are similar to baseline.

post-injection and one case was lost to follow up at only 6 months. The logMAR visual acuity equivalent was calculated and used for analysis (Table 1). The acuity was compared to MPS data for visual acuity in recurrent CNVM.[2]

RESULTS

The baseline pre-injection logMAR visual acuity averaged 0.94 (20/180 Snellen equivalent) and the mean final acuity was 1.00 (20/200) (Table 1). At 1 year, eight of 11 eyes were within 0.2 log units (approximately two lines of acuity) from baseline and one eye lost more than six lines of acuity. Of the eight phakic eyes, none had clinically significant progression of lens opacity. Three of 14 eyes required topical aqueous suppressants for mild elevation of intraocular pressure (in the 25 mm Hg range). In general, triamcinolone treated patients tended to demonstrate stability of vision and the neovascular lesion (Fig 1).

DISCUSSION

Within 2 years of laser treatment, 52% of extrafoveal CNVMs due to AMD will recur, usually on the foveal side of the laser scar.[1] Recurrence generally results in worse vision, with a mean acuity of 20/40 in those eyes without recurrence compared to a mean acuity of 20/125 in those eyes with recurrence at 1 year.

Table 1 Subjects' data

Subject	Last laser	Baseline		3 months		6 months		9 months		12 months		Cataract progress	IOP drug
		VA	LogMAR	VA	LogMAR	VA	LogMAR	VA	LogMAR	VA	LogMAR		
1	1 year	20/400	1.3	20/200	1.0	8/180	1.35	10/300	1.5			no	no
2	1 month	20/40	0.3	10/32	0.5	10/32	0.5			10/25	0.4	no	no
3	2 months	10/125	1.1	10/80	0.9	10/100	1.0	10/100	1.0	10/125	1.1	no	no
4	2 months	10/40	0.6	10/63	0.8	10/40	0.6	10/63	0.8	10/40	0.6	IOL	no
5, right eye	3 months	10/100	1.0	10/50	0.7	10/50	0.7	10/63	0.8			no	yes
5, left eye	1 months	10/40	0.6	10/100	1.0	10/63	0.8	10/80	0.9	10/63	0.8	no	yes
6	1 months	10/100	1.0	10/100	1.0	10/125	1.1	10/125	1.1	10/100	1.0	no	yes
7	5 months	10/100	1.0	10/125	1.1	4/400	2.0			4/400	2.0	no	no
8	8 months	10/125	1.1	10/100	1.0	10/125	1.1			10/125	1.1	no	no
9	6 months	9/300	1.5	10/160	1.2	10/125	1.1	10/125	1.1	5/400	1.9	IOL	no
10	7 months	10/100	1.0	10/125	1.1	10/80	0.9			10.63	0.8	no	no
11	1 months	10/160	1.2	10/80	0.9	20/400	1.3					no	no
12	3 months	10/25	0.4	10/20	0.3	10/20	0.3	10/20	0.3	10/20	0.3	no	no
13	4 months	10/80	0.9	20/300	1.2	20/300	1.2			20/400	1.3	no	no
	<4 months>		<0.94>		<0.91>		<0.99>				<1.0>		

Cataract progress (progression)=worsening of cataract at any time during follow up. IOL=intraocular lens. IOP drug=topical ocular antihypertensive administered for intraocular pressure >25 mm Hg.

The present study is a consecutive case series and the results can only be considered suggestive. However, since the inclusion criteria for patients from the subfoveal recurrence arm of the MPS study were similar and the visual acuity measurements were standardised and similar between studies, it is of interest to compare visual outcome in these triamcinolone treated eyes with the MPS cohort receiving repeat photocoagulation for subfoveal recurrence.

The follow up MPS study randomised eyes with recurrent subfoveal CNVM post laser to subfoveal laser treatment or observation.[2] Eyes receiving laser had an early abrupt decrease in mean acuity, from 20/125 at baseline to 20/250 at 3 months, but mean acuity was stable thereafter through 24 months of follow up. MPS observation group eyes had better mean acuity at 3 months (20/200), but by 1 year had acuity worse than the laser treated group (about 20/320) and this was grossly stable through the 24 months of follow up. The baseline acuity in the current study was slightly worse than in the MPS cohort (20/180), but the final acuity at 1 year was similar to laser photocoagulated subfoveal recurrences (20/260) and better than in the MPS observation group.

This series suggests that intravitreal TAAC may be an alternative treatment for patients with subfoveal recurrence after laser photocoagulation of extrafoveal CNVM in AMD for those patients refusing further laser treatment. Advantages include ease of administration and avoidance of early persistent vision loss associated with photocoagulation of the foveal region. Patients receiving this treatment must have careful follow up for possible steroid induced IOP increases, seen in about 30% of patients in previous reports.[8 9] This is an incidence consistent with topical, systemic, or sub-Tenon injection steroid use.[9]

Further randomised studies will be necessary to determine whether TAAC injection has a role as a first line treatment for subfoveal recurrence, how it compares with other emerging and investigative treatments of CNVM that have not yet been tested in such patients (such as photodynamic therapy, transpupillary thermotherapy, radiation therapy, and use of other antiangiogenic agents), or whether it has value as an adjuvant agent in combination with another investigational therapy.

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