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CLINICAL STUDY

Intravitreal triamcinolone will cause posterior subcapsular cataract in most eyes with diabetic maculopathy within 2 years

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Abstract

Purpose **To determine the incidence of cataract following intravitreal triamcinolone (IVTA) for diabetic macular oedema.**
Methods **Prospective, non-randomised, interventional cohort case series. A total of 27 eyes of 27 patients with diabetic macular oedema received an intravitreal injection of 4 mg (0.1 ml) of triamcinolone acetonide inferotemporally through the pars plana under direct vision. In 20 patients the fellow eye served as control, whereas seven patients had both eyes injected (not simultaneously). Seven patients had a repeat (second) injection in the same eye. The main outcome measures were cataract and intraocular pressure (IOP) rise of at least 5 mmHg (IOP responder).**
Results **The mean follow-up time was 18.9 months (range 13–29 months). A total of 22 (81%) of 27 eyes developed cataract during the follow-up period, of which 20 (74%) were posterior subcapsular in nature. None of the 20 uninjected fellow eyes developed posterior subcapsular cataract. Mean time to cataract formation was 16.2 months. In the seven patients who had both eyes injected, mean time to cataract formation was 16.5 and 17.1 months in the first and second eye, respectively. Mean time to cataract formation in seven eyes receiving a repeat second injection was 17.9 months. There was no significant difference in cataract formation between IOP responders (85%) and non-responders (79%) ($P = 1.00$, Fisher's exact test). Uneventful cataract surgery was performed in six eyes of five patients.**
Conclusion **This study demonstrates that given appropriate long-term follow-up, the majority of patients, even after a single IVTA injection, will go on to develop cataract, of which posterior subcapsular will be by far the most common.**

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Introduction

Intravitreal triamcinolone (IVTA) is now a well-established treatment for diabetic macular oedema both with[1–3] and without [4,5] prior macular laser treatment.

Since June 2002, we have been using IVTA in the treatment of diabetic macular oedema.[6,7] A well-known complication of steroid usage is cataract formation and in particular posterior subcapsular cataract (PSC).[8] This study reports the results of clinical observation on a cohort of patients who had IVTA injected to manage diabetic macular oedema in phakic eyes.

Materials and methods

The records of all patients treated with IVTA for diabetic macular oedema between June 2002 and April 2005 were examined. A total of 30 eyes of 30 patients were identified. Of which three patients had type I and 27 had type II diabetes mellitus. The following parameters were recorded before and following treatment;

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LogMAR best-corrected visual acuity, corrected reading ability, lens status (clinical examination by slit-lamp following dilation), intraocular pressure, and central macular thickness using Ocular Coherence Tomography (Stratus/Zeiss OCT III), when this instrument was introduced into our department. Following treatment, patients were reviewed at 1 week, 1 month, 3 months, and at 3-monthly intervals following this.

Only 27 patients were included in the analysis as one patient had died, one was lost to follow-up at 3 months and one had cataract formation that was inconclusive from the medical records.

In 20 patients the fellow eye served as control, while seven patients had both eyes injected (not simultaneously). Seven patients had a repeat (second injection) in the same eye. Where a patient had both eyes injected, only the first injected eye was included in the analysis.

Informed consent was obtained from each patient. The eye was injected with 0.1 ml (4 mg) of triamcinolone acetonide (Kenalog 40; Bristol-Myers Squibb). The method of injection is as in our previous papers.[6,7]

Results

The mean age of the patients was 67. 6 years at injection, with a range of 32–80 years. A total of 22 (81%) of 27 eyes developed significant cataract, with 20 (74%) of the 27 eyes developing PSC. Five (19%) of 27 eyes did not develop cataract during the follow-up period (Figure 1). One patient was lost to regular follow-up 3 months postinjection, but had developed a dense white cataract when they were next seen (17 months postinjection). One patient developed cataract (between 12 and 15 months postinjection) and went on to have cataract surgery but the case notes did not state the type of cataract.

None of the 20 uninjected fellow eyes developed PSC or other significant cataract. The time to first documentation of significant cataract was 16.2 months, with a range of 3–29 months. A total of 13 eyes showed a significant IOP rise (defined as an IOP rise $\geqslant$5 mmHg) on at least one postinjection visit, whereas 14 eyes did not. There was no significant difference in cataract formation between IOP responders (85%) and non-responders (79%) ($P=1.00$, Fisher's exact test).

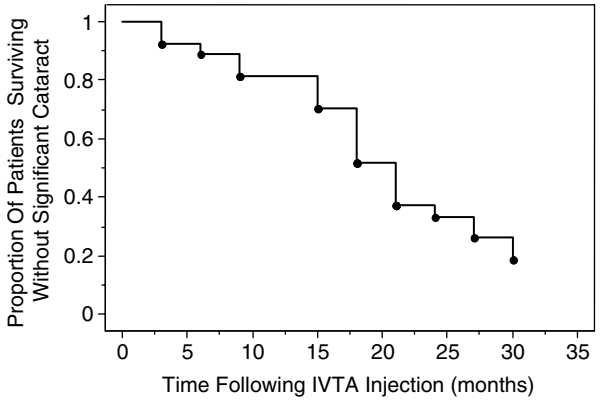

Figure 1 Kaplan–Meier survival plot indicating likelihood of remaining cataract free following intravitreal injection of triamcinolone.

In the seven patients who had a repeat (second) injection in the same eye, mean time to second injection was 10.4 months, with a range of 4–16 months. Time to first documentation of significant cataract ('Significant cataract' - cataracts observed in this study considered to have a significant effect on vision in the absence of macular pathology) was 17.9 months from first injection. This is actually a longer average time than those eyes that received a single injection (16.2 months), perhaps indicating that it is the first injection that is the most cataractogenic.

In the seven patients who had both eyes injected (not simultaneously), six of seven second eyes developed PSC. Mean time to cataract formation in the second injected eye was not significantly different at 16.5 months, whereas in the first injected eye it was 17.1 months.

Six (22%) of 13 IOP responders developed raised IOP considered to require treatment. In all cases, the IOP was adequately controlled with topical glaucoma medication, with some patients requiring oral acetazolamide for a short period of time. Four (67%) of these six eyes developed PSC. The remaining two eyes did not develop cataract. The mean time to cataract formation in the four raised IOP responder eyes requiring treatment was 14.25 months (SD = 7.0 months). Twenty-one (78%) of the 27 eyes did not develop raised IOP requiring treatment. Sixteen (76%) of these 21 eyes developed PSC. Time to cataract formation in these eyes was 17.7 months (SD = 7.6 months). There was no significant difference in cataract formation between IOP responders requiring treatment (67%) and those not requiring treatment (76%) ($P=0.63$, Fisher's exact test).

The only other complication of IVTA injection was in a warfarinised patient who developed a subconjunctival haematoma, which eventually required surgical excision.[9]

Discussion

Formation of PSC is a well-known side effect of corticosteroids, whether administered by topical, systemic,[8] or intravitreal route.[13]

To the best of our knowledge, previous studies from other authors investigating the role of IVTA in the treatment of diabetic macula oedema have followed patients for a relatively short time only, with mean follow-up times varying from 3[3] to 11.7 months.[11] Consequently, this has not given investigators the opportunity to identify the long-term sequalae following IVTA, in particular, significant cataract formation.

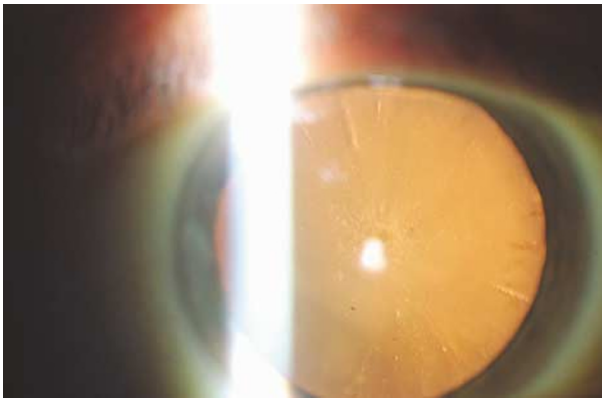

Figure 2 Slit lamp photograph of a typical posterior subcapsular cataract seen to develop following intravitreal injection of triamcinolone.

Some studies report no cataract formation 6 [2] and 10[4] months post-IVTA. One study with a 3-month follow-up reports cataract formation in 3% of patients.[3] Studies with a 6-months follow-up report varying rates of cataract formation. 3.8,[10] 6.25,[1] 6.7[11] and 17%,[12] all much lower than in our prospective case series. One paper[13] found that 24% of eyes treated with IVTA developed cataract by 2 years, but this was when IVTA was used as a treatment for ARMD and not diabetic macular oedema. PSC, even at an early stage, can be very detrimental to visual function and can render OCT scanning ineffective. This is important as OCT is used to monitor central macular thickness and architecture, as well as to determine the need for further treatment. We have noticed that early PSC results in poor-quality OCT scans.

One weakness of this study is that cataracts were graded without the use of any classification system, such as the LOCS system. The cataracts were graded by any one of the three authors. However, all PSCs observed in this study were considered to have the potential to have a significant effect on vision (Figure 2).

We found no significant difference in cataract formation between IOP responders (85%) and non-responders (79%). This contradicts the findings of Gillies *et al*,[14] who found a significant difference in cataract formation in non-diabetic eyes between IOP responders (51%) and non-responders (3%) after 2 years. We therefore do not support the view that PSC is unlikely to develop in eyes that do not experience elevated IOP after IVTA. As we have not found an association between IOP and PSC, the mechanisms for development of steroid-related cataract and raised IOP are likely to be different in diabetic eyes.

One could postulate that the high rate of cataract in our series is owing to our injection technique but this is unlikely, as we have followed a standardised protocol for IVTA injection.[1]

It is interesting to note that IVTA is being used as a primary treatment for diabetic macular oedema[4,5] and that The National Eye Institute, US, is performing a randomised controlled trial comparing macular laser treatment *vs* IVTA.[15] This will inevitably lead to almost every treated eye developing sight-threatening cataract.

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