The problem of pressure elevation associated with intravitreal triamcinolone

M D Conway

A question remains about the relation between the amount of drug in the vitreous cavity and the intraocular pressure elevation and duration

Intravitreal triamcinolone acetonide (IVTA) has increasingly been employed as a treatment for various intraocular inflammatory, neovascular, exudative, proliferative, and oedematous conditions.^{1–46} The injection usually results in transient improvement in visual acuity but repeated injections are usually required because the vision increases and eventually decreases again.^{8–10 19 21 43 45}

Repeated IVTA injections have sparked investigations into the both dose response and quantification of the post-IVTA intraocular pressure rise.^{12 39 42 43} Although 4–8 mg doses drawn undiluted from the commercially available vial are commonly used, some investigators wash the diluent from the commercially available medication and concentrate it into a 20–25 mg dose in a small volume.^{10–12 16 21–24 39 40 42–46} In terms of the duration of the IVTA effect and improved retinal thickness there is definitely a dose response,³³ and enhanced vision in eyes with diffuse diabetic macular oedema has been directly linked to the dose of drug by Spandau *et al.*^{21 28} Jonas *et al* have also demonstrated that the peak in visual improvement chronologically parallels the peak in the IOP measurement and occurs 2–5 months after injection.²¹ Clearly the duration of that improvement may be dose related with the 20 mg doses lasting 6–9 months and the 4 mg doses lasting 2–4 months.^{7 46} Unfortunately, the relatively immediate and somewhat dramatic initial visual improvement may be followed by a smaller incremental improvement with each subsequent injection.⁸ A question remains about the relation between the amount of drug in the vitreous cavity and the intraocular pressure elevation and duration.^{12 24}

In the past, the secondary ocular hypertension complication of IVTA was reported in 28%–77% of eyes injected after a single dose. In this issue of *BJO*

(p 999), Rhee *et al* report a 53.2% prevalence of any IOP elevation in eyes following a single IVTA injection, 50.6% of which were at least 30% above baseline.⁴⁷ Additionally, they report that 65.1% of eyes that received a second injection demonstrated a 30% increase over baseline. In a prospective study using 25 mg doses, Jonas *et al* reported that in about 50% of eyes, IOP elevation occurred about 2 months after the injection¹² and both Jonas and Park have reported that a younger age is a risk factor for a significant IOP spike post IVTA.^{12 41–43} Additionally, Rhee *et al* report here⁴⁷ that a baseline IOP of 16 mm Hg or above and eyes receiving a second injection may be other risk factors for a significant IOP rise similar to that previously reported by Jonas.^{12 47}

In attempting to predict which eyes may be prone to IOP elevation post IVTA, two strategies have been reported with some important conclusions. In this report by Rhee *et al* and a previous report by Feistmann *et al*, pretreatment with frequent (up to hourly) topical prednisolone acetate 1% did not correlate with an IOP rise post IVTA, indicating this is not a good provocative test.^{38 47}

The recommendation that patients should be monitored for an extended period of time after IVTA injection is very important

A more predictive test was reported by Bhavan *et al* and in our other studies where a test dose of 400 µg of IVTA provoked an elevated IOP in 8–15% of non-glaucomatous eyes within 1 week following IVTA and 33% of eyes with pre-existing glaucoma.^{35 36} This provides a useful test to select eyes with a propensity to develop significant IOP elevation post-IVTA. The appeal of this provocative test is that while the test dose of drug allows some immediate

improvement in vision (the desired outcome), the smaller dose (one tenth of the 4 mg dose) has a diminished duration in case the IOP becomes elevated. Additionally, we found that after successfully tolerating the 400 µg test dose, 50% of eyes receiving an 8 mg dose of IVTA had a late IOP spike (2–5 months) compared to 12% of those receiving a 4 mg dose. This suggests that pre-existing glaucoma and an 8 mg dose may be relative risk factors for post-IVTA IOP spikes.^{35 36} Identifying these “at risk eyes” may be extremely important since susceptible optic nerves may tolerate less elevation of pressure safely.

The fallacy of all provocative testing is that the duration of the drug is variable (perhaps remaining measurable up to 18 months following a single injection²⁴) and possibly is cumulative, and despite a normal IOP on provocative testing, many eyes still have a significant IOP elevation at 6–9 months.^{24 35 36 40} This elevated rate of IOP rise with repeated injections is significant considering that the drug may be given every 1–3 months in some disease processes.

In conclusion, the recommendation by Rhee *et al* that patients should be monitored for an extended period of time post-IVTA injection is very important. Eyes at increased risk for post-IVTA elevation of IOP include those with a baseline IOP >16 mm Hg, younger age, repeated IVTA injections, pre-existing glaucoma, and an increased IOP following provocative testing with a 400 µg test dose. Larger doses of drug last longer. IOP spikes may occur 2–9 months after IVTA injection and measurable drug may be present for up to 18 months.^{7 12 24 24 35 36 39 46 47}

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Correspondence to: Professor Mandi D Conway, University of Arizona Health Sciences Center, Department of Ophthalmology and Vision Science, 655 N Alvernon Way, Suite 108, Tucson, AZ 85711, USA; mconway1@tulane.edu

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