Intravitreal Triamcinolone Acetonide for Diabetic Macula Edema

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In their very interesting paper, Desatnik et al. [1] report that intravitreal injection of triamcinolone acetonide is effective in reducing foveal thickness and improves visual acuity in the short term, but that visual acuity returned to pre-injection values and only a moderate reduction in foveal thickness persisted.

Macular edema is a common cause of visual loss in diabetic retinopathy, occurring in about one-third of affected individuals with long disease duration [2]. IVTA treatment of diabetic macular edema unresponsive to conventional grid laser therapy was pioneered by Jonas and Sofger [3], who reported their findings in 2001. This publication motivated numerous clinical series that evaluated the efficacy and safety of IVTA for diabetic macular edema [4-10]. Most of the series published in the ophthalmology literature showed the same trend of a rapid improvement phase and stabilization for several months, followed by regression to baseline or near baseline visual acuity in most eyes, as now shown by Desatnik and co-workers [1].

The drug is conveniently available in concentrations of 40 mg/ml in a sterile preparation (Kenalog®, Bristol-Myers Squibb, USA) and is commonly used in other specialties, such as orthopedics, for treating inflammatory processes. We usually inject intravitreal drugs up to a volume of 0.1 ml without causing an unacceptable pressure elevation, and this is the maximum dose we can inject from the available preparation of TA. It is possible that the dosage of the injected drug determines the duration of its effect in eyes. All of Desatnik's patients received a single 4 mg (0.1 ml) injection [1].

There is currently an ongoing 6 month prospective, randomized, dose-escalation trial – the ISIS trial – for evaluating 2 mg/0.05 ml vs. 4 mg/0.1 ml IVTA in diabetic macular edema. Preliminary results presented at the 2005 Academy meeting demonstrated resolution of macular edema in 38% of the treated eyes at 3 months and in only 19% of the treated eyes at 6 months, suggesting a recurrence rate of approximately 50%. There was a trend toward the 4 mg dose having greater efficacy and longer duration. A subgroup analysis revealed that 62% of subjects (8/13) with a cystoid pattern of angiographic leakage had a gain of three lines or more of vision, compared to only 9% (1/11) of those with non-cystoid angiographic leakage. Martidis and associates [11] reported a small series of patients receiving IVTA for refractory macular edema: three of eight eyes were reinjected after 6 months because of recurrence of macular edema. Massin et al. [12] prospectively evaluated the effect of a single IVTA 4 mg injection in one eye compared to the control fellow eye in 15 patients with bilateral diabetic macular edema unresponsive to laser treatment. There was a significant decrease in macular thickness in favor of the injected eye after 3 months, but that difference was no longer significant after 6 months due to recurrence of macular edema. Spandau and colleagues [13] compared the safety and efficacy of injected 2, 5 and 13 mg IVTA and found significantly improved outcome in terms of visual acuity and duration of the effect of IVTA in the 13 mg group. Jonas et al. [14] conducted a large prospective comparative study on 166 eyes of 136 patients and reported a significant increase in visual acuity in eyes assigned for IVTA 20–25 mg compared to eyes assigned for laser treatment. All these findings indicate the possibility that increased dosage will result in improved long-term results. Although other relevant studies in the literature failed to arrive at any firm conclusions due to the use of different criteria (i.e., with or without previous macular laser, varying durations of edema, absence of baseline visual acuity), it is still very likely that there is a longer lasting effect associated with a higher TA dose.

There are other questions concerning IVTA in diabetic macular edema that remain unanswered. For example, it is not clear what is the optimal timing of TA injection with respect to the latest focal laser treatment, nor the optimal timing for reinjection. Avitabile et al. [15] showed better visual acuity outcome and lower central macular thickness in 22 eyes that received IVTA 4 mg compared to 21 eyes that received grid laser treatment. Patelli and team [16] reported that IVTA was effective in reducing macular thickness and improving visual acuity in eyes with and without previous laser treatment, but stated that it is not yet clear whether IVTA should be considered as an initial treatment. It is possible that the decision to inject and reinject is influenced by angiographic features (e.g., the existence of macular non-perfusion, the existence of cystoid spaces) [17] or optical coherence tomographic features [18]. These questions remain unanswered primarily due to the lack of data: most series include relatively small numbers of treated patients, lack a control group, are not randomized and have short-term follow-up.

In analyzing the benefits of IVTA, we would be remiss to ignore the well-established side effects following injection, such as increased intraocular pressure (occurring in 35–50% of cases) [15,19,20], progression of cataract [15], and infectious and non-

IVTA = intravitreal injection of triamcinolone acetonide

infectious endophthalmitis [21]. Jonas et al. [22] estimated the rate of infectious and non-infectious endophthalmitis to be 1:1000 after IVTA using filtered triamcinolone free of the solvent agent and suggested a protective effect when removing the solvent prior to injection.

Taken together, the findings from currently available studies preclude the drawing of definitive conclusions and treatment guidelines. Our role as ophthalmologists is to offer our patients the best available treatment suitable for them. When conventional treatment is no longer efficacious, we may consider suggesting new treatments with short-term benefits after carefully weighing the benefits against possible untoward side effects. The subject of IVTA injection in patients suffering from diabetic macular edema requires much more research, and probably a large, multicenter, controlled, randomized clinical trial to establish its cost-effectiveness, clinical utility, timing and indication for injection and reinjection, long-term efficacy and complications.

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If you came home and found a strange man… teaching your kids to punch each other, or trying to sell them all kinds of products, you'd kick him right out of the house, but here you are; you come in and the TV is on, and you don't think twice about it.

Jerome Singer, U.S. child psycologist and educator