

Considerations for Intravitreal Triamcinolone Use

Because ocular injection of this treatment is an off-label use, physicians must consider associated complications and the importance of informed consent.

BY LAURA SUAREZ, MANAGING EDITOR

The corticosteroid triamcinolone (Kenalog) interferes with chemical reactions that cause inflammation, redness and swelling in the body. It is approved by the Federal Drug Administration (FDA) for topical use; it is often used for treating allergic reactions, eczema and psoriasis.¹ It is not, however, FDA approved for intraocular use. In fact, according to Drugs.com, contact with the eyes should be avoided. So, why then, do retina specialists commonly use it intravitreally to treat retinal disease, especially when it may be associated with a slew of complications including endophthalmitis, pseudoendophthalmitis, sterile endophthalmitis, elevated IOP, cataract and glaucoma?

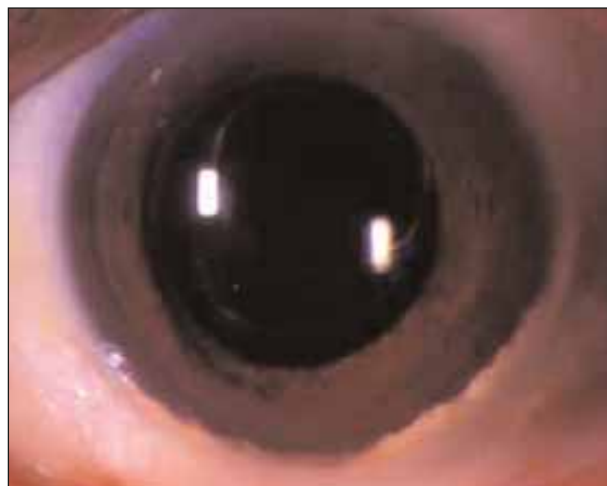
According to Nancy M. Holekamp, MD, triamcinolone may have beneficial effects when injected into the eye. More specifically, intravitreal steroid injections may provide patients with a temporary improvement in vision. Currently, there are no large, randomized, prospective clinical trials that confirm this benefit, she said, but practicing retina specialists believe their patients are better off. Interestingly, other off-label intravitreal treatments such as bevacizumab (Avastin; Genentech, San Francisco, Calif) are also gaining popularity because of that same effect on vision, as current standard of care therapies do not improve vision but rather primarily avoid further vision loss.

The function of focal laser treatment — the standard of care for diabetic macular edema (DME) over the past 30 years and branch retinal vein occlusion (BRVO) for approximately 25 years — is to stop leakage. For DME, visual

improvement is possible, but not the goal of treatment. For BRVO, the average patient only experiences a 1.3- to 1.7-line improvement in vision with focal laser treatment.² For central retinal vein occlusion (CRVO), laser surgery is not beneficial for the associated macular edema. Recent small retrospective series and case reports have shown that intravitreal corticosteroids may offer some short-term visual improvements in patients with DME, BRVO and CRVO. The long-term benefits are less certain; they require further study. In patients with macular degeneration, intravitreal corticosteroid use may enhance effects of photodynamic therapy. According to Dr. Holekamp, this may mean fewer treatments and better outcomes.



Figure 1. Endophthalmitis may occur after an intravitreal injection of triamcinolone.



Figures 2,3. Pseudoendophthalmitis occurs when the steroid migrates into anterior chamber (pseudophakes) and mimics infection. Gram stain and lack of symptoms can help distinguish diagnosis.

Dr. Holekamp is from the Barnes Retina Institute, St. Louis. She regularly uses triamcinolone as a salvage therapy when patients fail standard of care or if no standard of care is approved. The only absolute contraindication is sensitivity to triamcinolone or the preservatives found in triamcinolone. A strong relative contraindication exists when triamcinolone is used in glaucoma patients because there is overlap between steroid responders and patients with glaucoma. A large percentage of glaucoma patients will develop elevated IOP after intravitreal triamcinolone injection.

"I use [triamcinolone] if my patient has failed standard therapies," she said, adding that it is important to obtain informed consent. "The patient and I decide together that we should give it a try. That is the art of medicine: deciding when to use something that is not [FDA] approved and has a significant risk profile."

The purpose of informed consent is to communicate to the patient the benefits, risks and alternatives associated with any treatment. The risk/benefit ratio is generally established by clinical trial data, however, no trials exist for intravitreal triamcinolone use. Practicing physicians must be aware of the reported literature and discuss the balance of risks and benefits with each patient. Not every patient will accept the following probable risks of triamcinolone: 50% chance of cataract progression within 1 year; 30% to 40% chance of elevated IOP; 1% to 2% chance of glaucoma surgery; and <1% chance of endophthalmitis (Figure 1).

PRESENT COMPLICATIONS

"One problem with the rapid and widespread use of [triamcinolone] is that no one had a true appreciation for the complications," Dr. Holekamp said in an interview with *RETINA TODAY*. "Doctors are very eager to use something new, particularly if they and their patients are seeing visual

improvement in the short-term, but very few do the painstaking clinical research to discover what the complications are."

Associated risks were not truly appreciated until 4 or 5 years after triamcinolone came into widespread use in 2001, Dr. Holekamp said. Now that they are known, informed consent should become an integral part of triamcinolone treatment. In her opinion, informed consent for intravitreal triamcinolone should include the following information:

- Triamcinolone is not formulated for injection into the eye;
- Triamcinolone is not FDA approved for injection into the eye;
- No evidence in the form of large, randomized prospective clinical trials shows that triamcinolone is beneficial, although it is believed to be beneficial;
- Effects of triamcinolone are temporary and generally last 6 months. To be continuously beneficial, repeated injections are needed; and
- Use of intravitreal triamcinolone includes the following risks: endophthalmitis, pseudoendophthalmitis, sterile endophthalmitis, elevated IOP, cataract, glaucoma, retinal detachment and vitreous hemorrhage.

Pseudoendophthalmitis occurs if triamcinolone shifts into the anterior chamber in pseudophakes (Figures 2,3). In this instance, the steroid particles imitate infection. The incidence of pseudoendophthalmitis is rare. In one reported series, only 0.8% of eyes injected with intravitreal triamcinolone developed this complication.³ Moshfeghi et al discovered that crystals suspended in both the aqueous and vitreous were noticeable 3 days postinjection. By 14 days postinjection, crystals disappeared without sequelae.

Sterile endophthalmitis is another uncommon complication. In one series it was present in approximately 7% of

injected eyes.⁴ Pain is not commonly associated with this condition, although inflammation may be present between 1 and 2 days postinjection. Patients who experience sterile endophthalmitis may experience a decline in vision to 20/400. They will generally return to preinjection levels.

The complications of pseudoendophthalmitis or sterile endophthalmitis associated with intravitreal injection were noted in the early days of triamcinolone use. This diagnosis was made as early as 1 to 3 days postinjection. Because most physicians are comfortable with giving intravitreal triamcinolone injections, they do not see their patients until 7, 14 or 28 days after injection and may not be aware of the presence of these conditions, Dr. Holekamp said.

"These two diagnoses are important because you need to differentiate them from endophthalmitis, which is devastating and can lead to total loss of vision," she said. "As a physician — in the case of pseudoendophthalmitis — you must be able to say, 'This is going to get better on its own,' or — in the case of true endophthalmitis — 'You need emergency intravitreal antibiotics and you are at great risk at losing not only vision but your eye.'"

Perhaps the most potentially devastating complication associated with intravitreal triamcinolone is endophthalmitis. According to the first reported series of intravitreal triamcinolone studies associated with endophthalmitis, 0.87% of 922 eyes developed this complication.⁵ It is suggested that triamcinolone alone may be a risk factor for increased incidence of endophthalmitis. In a rabbit model study involving 40 eyes (20 injected with bacteria plus triamcinolone and 20 injected with bacteria alone), it was determined that intravitreal triamcinolone was associated with a greater risk of infection.⁶ Of the rabbit eyes, 85% injected with bacteria plus triamcinolone and 30% injected with bacteria had a culture positive rate. All rabbit eyes injected with triamcinolone developed endophthalmitis.

Elevated IOP and possible glaucoma are not infrequently associated with intravitreal corticosteroid injection. In a comparison of 75 eyes treated with intravitreal steroids and 76 control eyes, 41% versus 4%, respectively developed elevated IOP.⁷ Generally, IOP peaks early and gradually normalizes over 6 to 9 months. The degree of elevated IOP may vary. Jonas et al⁸ reported that among 305 eyes, IOP readings ranged from >21 mm/Hg to >40 mm/Hg. Patients who have a history of glaucoma or have taken glaucoma medication are at a higher risk of developing glaucoma after intravitreal steroid injection. Other risk factors for glaucoma include a baseline IOP >15 mm/Hg, younger patients and concurrent posterior subcapsular cataract (PSC).

Increased progression of cataract may also occur after intravitreal steroid injection. In one study, PSC cataract showed significant progression in 45% of eyes 12 months postinjection.⁹ Younger patients may be less susceptible to

the development of PSC cataract. This complication occurred even with a single injection of steroid. Nuclear sclerotic cataract did not significantly progress unless multiple triamcinolone injections were given. According to Dr. Holekamp, these data suggest that even one injection of triamcinolone may cause increased susceptibility to cataract.

Patients only know about the potential of these complications if informed consent is thorough and complete, Dr. Holekamp cautioned. "Every physician should discuss these risks," she said. "You can talk patients into anything if you tell them that they are going to get better but omit talking about the side effects."

Also, if patients know what to expect, they are less likely to be unhappy if a complication occurs, Dr. Holekamp said. "When you are doing something surgical — like an injection — and you are doing something that is not FDA approved and not even validated by randomized, prospective, clinical trials, the bar is really very high for informed consent."

Triamcinolone is inexpensively manufactured and pharmaceutical companies do not make a lot of money on its production, Dr. Holekamp said. The cost to patients and physician practices is low. Because triamcinolone is so widely used, recently a nationwide shortage of triamcinolone was reported. This shortage is likely to be short-lived, as physicians are also using bevacizumab (Avastin; Genetech, San Francisco) off-label for intravitreal injection. According to Dr. Holekamp, bevacizumab may not carry with it the complications of cataract and glaucoma. "We may actually see [triamcinolone] use decrease because of [bevacizumab], but that is always in flux. How frequently I use [triamcinolone] today may differ 6 months from now." Dr. Holekamp will, however, continue using informed consent with any intravitreal steroid injection. ■

Nancy M. Holekamp, MD, is from the Barnes Retina Institute, St Louis. She can be reached at nholekamp@pol.net.



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