Intravitreal injection procedures have been performed in exponentially increasing numbers since 2004 due to availability of a greater number of drugs for a wider array of indications. It is estimated that nearly 6 million intravitreal injections have been performed in the United States alone, making it one of the most commonly performed procedures in all of medicine.

Eric M. Shrier, DO, and Joseph Raevis, MD, from New York provide us with a very interesting and concise review of how to decrease the risk of the intravitreal injections while maximizing patient comfort. Despite the high number of intravitreal injections performed, it is fascinating to see that there is no “one best way” to perform the procedure based on what is found in our literature.

Drs. Shrier and Raevis remind us of the importance of our community sharing ideas and learning from each other with the goal of helping our patients. The intravitreal injection procedure has clearly evolved during the last one to two decades due to our colleagues trying to perfect the procedure. Just in the past decade, our practice has decreased antibiotic use, implemented a “no-talk policy,” and started using smaller needles. I am certain their review will be a welcome reminder to those who read it of how important this procedure is in the management of a wide variety of retinal diseases.

**INTRODUCTION**

Intravitreal injections (IVIs) are one of the most common surgical procedures performed in the world, with an estimated 5.9 million IVI in the United States in 2016. These injections are the foundation of modern retinal treatment and are used in a wide variety of disorders such as diabetic retinopathy, exudative macular degeneration, and retinal vein occlusions.

The injection techniques vary among injectors, with the goal being prevention of infectious endophthalmitis (IE) while providing for patient comfort. IE is rare after IVI, with an incidence of only 0.028% (1/3,544), but it is the most feared complication of IVI due to the potential for devastating outcomes, even with prompt treatment. We briefly summarize the evidence for different techniques of providing IVI in a safe and comfortable manner.

**PRE-PROCEDURE ANESTHESIA**

Patient comfort is of the utmost importance since many patients will need to receive many IVIs to have maximal visual benefit. Thus, the goal of any technique is to increase compliance through comfort. Methods of anesthesia include topical proparacaine, tetracaine, lidocaine gel, soaked pledgets, and subconjunctival lidocaine injection. All of these methods have been shown to have a relatively low level of associated pain. A subconjunctival injection of 2% lidocaine has been shown to have benefit for certain patients who are sensitive to pain; however, this technique requires a second injection.

It should be noted that when anesthetic gel is used, povidone iodine (PI) should be applied to the ocular surface prior to application of the gel to prevent bacteria from being sequestered by the gel.
TOPICAL ANTIBIOTICS

No trial has demonstrated benefit with topical antibiotics and, thus, they are not presently recommended. The incidence of IE has been shown to increase with topical antibiotic prophylaxis. It is hypothesized that antibiotic use increases resistance of the ocular flora or that the repeated use of antibiotics, such as fluoroquinolones, have a detrimental effect on the ability of the ocular surface to prevent infection.

SURGICAL MASK

Injection-related IE is most commonly from Staphylococcus and Streptococcus species. Streptococcus is not normally found on the ocular surface, yet it is found in the normal flora of the upper respiratory tract and oral cavities. That is why it has been hypothesized that oropharyngeal droplets could be the origin of these cases of endophthalmitis. This is supported by the fact that post injection IE with streptococcal isolates after IVI are approximately three-times more prevalent than when compared to intraocular surgery performed in an operating room. In light of this, a face mask should be considered or a no-talk policy be instituted during the setup and injection to help prevent aerosolization of oropharyngeal pathogens from contaminating the IVI.

GLOVES

Hand hygiene is essential before every patient contact, but there is a significant variation with the use of gloves for IVI. In the United States, 27% percent of physicians use no gloves at all during IVI. There are no studies that show decreased rates of IE with the use of sterile or nonsterile gloves. In our experience, the use of gloves seems sensible but not necessarily mandated by the evidence in the literature.

TOPICAL ANISEPSIS

PI is considered standard of care due to its effectiveness, low cost, and low incidence of microorganis-
ism resistance. PI has broad-spectrum microbicidal activity and has been shown to be bactericidal in as short as 30 seconds for concentrations between 2.5% to 10%. Most physicians use 5% PI on the ocular surface; however, with sensitive patients, it has been documented that 1.25% PI is safe, as well. Periocular lid scrubs with PI are not recommended.

Irritation from PI is the most common complaint, and patients may develop a contact dermatitis, but there have been no reported cases of anaphylaxis due to PI during ophthalmic use. If a patient has anxiety, we offer to place a drop of PI on the back of their hand or forearm for 5 minutes and let them observe if a reaction will occur. Prior to attempting a subsequent injection, this sometimes alleviates their anxiety and improves compliance in our experience.

As an alternative to PI, chlorhexidine gluconate (0.1%) may be used and well tolerated with comparably low IE rates to PI. Clinical studies on the ideal ocular contact time have yet to be established.

EYELID RETRACTION

Eyelashes and the eyelid margin are a main source of infection with ocular procedures, so it is essential to have them retracted during IVI to ensure the needle or ocular surface not be contaminated. An eyelid speculum is a commonly used method; however, more comfortable methods exist such as the bimanual or unimanual cotton-tipped applicator and lid-splinting techniques (Figure 1).

Some physicians in our practice use the cotton-tipped applicator methods for eyelid retraction technique, and we have shown these methods to be significantly more comfortable than a speculum in a prospective, randomized study (unpublished data). With a visual analog scale (VAS) of pain, which ranges from 0 (no pain) to 100 (worst pain), we were able to show that eyelid retraction with a speculum had a VAS of 18, unimanual had a VAS of 6.5 VAS, and the cotton-tipped applicator method of eyelid retraction had a VAS of 8.

Eyelid retraction with speculum is known to be more uncomfortable than less-invasive methods of eyelid retraction. The main driving factor to not using a speculum is patient comfort.

LOCATION

IVI are commonly placed in the superior temporal and inferior temporal quadrants; however, they may be placed safely when performed 360° through the pars plana. Injections in the each of the four quadrants have all been shown to be similarly comfortable. There is general agreement that injections should be placed posterior to the limbus less than 4.0 mm in phakic eyes, 3.5 mm in pseudophakic eyes, and 3.0 mm in aphakic eyes.

OTHER COMFORT MEASURES

Classical music before and during IVI has been shown to decrease anxiety during. Penetrating the sclera perpendicular rather than doing a tunneled injection causes less pain. Topical nonsteroidal anti-inflammatory drugs (NSAIDs) such as bromfenac and ketorolac have been shown to decrease the pain during the IVI, whereas bromfenac and nepafenac decrease post-injection pain at 6 hours. Studies have shown that needle diameter is correlated to discomfort during the injection process, with comfort levels improving as needle size decreases from 26 to 33 gauge.

CONCLUSIONS

IVI have become the most common intraocular procedure, surpassing even cataract surgery, which is why this topic is of such importance. There are many different techniques for doing these injections, many lacking randomized studies due to the enormous numbers required due to the low incidence of endophthalmitis. We present a concise, up-to-date review on the major methods to decrease the risk while attempting to maximize patient comfort.

REFERENCES

Practical Retina


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