

# EXPERT OPINION

1. Article
2. Conclusion
3. Expert opinion

## Topical anesthesia for intravitreal injection

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In-office intravitreal delivery of medications has currently become the standard of care treatment for a variety of ocular conditions, including age-related macular degeneration, diabetic eye disease, cystoid macular edema, and vascular occlusions. Patients undergoing an intravitreal injection procedure most commonly experience pain at the injection site, which has led physicians to explore the best means to decrease or to abolish pain sensation. Currently, no method of topical anesthesia prior to intravitreal injection administration has been proven to eliminate pain completely. Comparisons between different topical anesthetic agents have not yielded a consensus superior agent to be widely recommended for regular use. In order to minimize pain and reduce anxiety, addressing the patient's injection-related concerns is important.

**Keywords:** anesthetics, intravitreal injections, pain, topical anesthesia

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### 1. Article

Intravitreal delivery of medications has become the standard of care treatment for a variety of ocular conditions, including exudative age-related macular degeneration [1], cystoid macular edema [2], diabetic retinopathy [3], and endophthalmitis [4]. Over the past 10 years, the use of intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF), such as bevacizumab and ranibizumab (Genentech, San Francisco, California, USA) have increased drastically, with 816,923 intravitreal injections of either bevacizumab or ranibizumab given in 2008 for neovascular age-related macular degeneration alone [5]. The use of intravitreal injections is likely to increase even further with the aging population in the United States, as many of these patients need repeated injections for the treatment of their ocular disease [6]. For age-related macular degeneration, the number of patients affected is projected to increase from 1.75 million in 2000 to 2.95 million in 2020 [7].

Briefly, the intravitreal injection procedure consists of placing an eyelid speculum, disinfecting the ocular surface with 5% betadine, and injecting a medication into the vitreous, usually with a 30-gauge needle placed on a 1 cc syringe. Medications injected in this manner into the eye include anti-VEGF pharmacotherapy, antibiotics, and steroids. Patients may experience pain or discomfort at the site of injection during the intravitreal injection procedure. Because of this, intravitreal injections are performed under topical anesthesia, most often in an office-based setting. Methods of ocular surface anesthesia include topical drop/gel administration, peribulbar injection, subconjunctival injection, and a pledget soaked in anesthetic. The use of specific anesthetic varies, including lidocaine (Hameln Pharma, Hameln, Germany), xylocaine (Inox Industries, Ontario, Canada), proparacaine (Afine Chemicals, Hangzhou, China), or tetracaine (Hainan Zhongxin Chemical, Haikou, China).

Few studies comparing different anesthetic methods were published to date. In this issue, the authors of Randomized Clinical Trial of Two Anesthetic Techniques for Intravitreal Injections prospectively compared the effectiveness and safety profile

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**Article highlights.**

- Few studies evaluate different forms of intravitreal injection anesthesia.
- No single method of intravitreal injection anesthesia has been repeatedly proven superior.
- Other factors including repetitive injections, gender, and age influence pain experienced during intravitreal injection.
- Addressing the patient's injection-related concerns is crucial.

This box summarizes key points contained in the article.

of 4% lidocaine on a cotton swab to 3.5% lidocaine gel. They determined that both techniques were equally effective and yielded mild discomfort during the procedure and the next day, although some of their patients preferred the gel due to less ocular surface irritation. Their findings are in agreement with a previous study by Yau *et al.* that prospectively compared the effectiveness of three topical agents used for intravitreal injections including 0.5% tetracaine hydrochloride drops and a 4% lidocaine pledget, 0.5% tetracaine hydrochloride drops alone, or 4% cocaine drops alone. No statistical or clinical difference in patient pain experienced was demonstrated between the three anesthetic options [8]. A similar study conducted by Blaha *et al.* prospectively compared the effectiveness of 0.5% proparacaine, 0.5% tetracaine, 4% lidocaine pledget, and subconjunctival injection of 2% lidocaine for intravitreal injection in 24 patients. There was no statistical difference in pain control among the different anesthetic options although subconjunctival lidocaine injection had the most side effects (subconjunctival hemorrhage and the possibility of intravitreal injection of lidocaine) [9]. These results were consistent with the findings of similar study performed by Kozak in 2005 in which it was showed that lidocaine 2% gel provided satisfactory pain control and produced less chemosis and hemorrhage than subconjunctival anesthesia [10]. Finally, Davis *et al.* compared the cost and anesthetic effect of topical proparacaine drops, 4% lidocaine solution, and 3.5% lidocaine gel on pain and the overall injection experience in 120 patients, both of which were scored by the patient after the injection. Similarly, there was no statistically significant difference among these agents [11].

Interestingly, factors independent of the type of anesthetic used may influence pain experienced by the patient during

the intravitreal injection procedure. LaHood *et al.* divided 120 patients undergoing intravitreal injection into three groups, each receiving one of the following: topical gel (2% lidocaine), subconjunctival (1% xylocaine), and combination topical gel and subconjunctival anesthesia. Although, there was no difference at 24 h post-injection in pain sensation between the groups, the study demonstrated a statistically significant difference between the pain scores of patients receiving their first intravitreal injection compared to those receiving their second or more injections [12].

Rifkin and Schaal have shown in a prospective, randomized study that not only pain sensation decreases with each further injection but also that other factors are important in influencing a patient's comfort during intravitreal injection. Their study demonstrated that factors influencing pain scores significantly included improved vision from previous injection, female sex, and age > 65 years [13]. Rifkin and Schaal have also shown that pain from intravitreal injection can last between 3 and 7 days, and may be lessened in patients using topical ketorolac (Apotex, Westin, Florida, USA) eye drops [14].

## 2. Conclusion

To date, there has been no method repeatedly shown to be proven superior in controlling pain during an in-office intravitreal injection procedure. Furthermore, other factors unrelated to the type of anesthetic used have been shown to influence pain sensation during the procedure, including number of previous injections and other environmental factors.

## 3. Expert opinion

Minimizing pain experienced during intravitreal injections and addressing injection-related concerns demands physicians' attention in order to provide compassionate patient care. Explaining every step of the intravitreal injection procedure to the patient in a clear manner and answering all patient questions or concerns before proceeding is crucial in reducing patient anxiety, discomfort, and pain.

## Declaration of interest

The authors state no conflict of interest and have received no payment in preparation of this manuscript.

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