

Ocular desensitization in the face of local anesthetic hypersensitivity

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Clinical Implications

- True hypersensitivity to local ester and amide anesthetics is extremely rare. This is the first documented case of successful ocular bupivacaine desensitization in a patient with suspected local anesthetic hypersensitivity.

TO THE EDITOR:

Local anesthetics (LAs) have been used in medicine since 1884 when Carl Koller applied cocaine to the cornea.¹ Hypersensitivity reactions to LAs have been associated with a metabolite of ester group anesthetics as well as components found within the LA solutions.² True IgE-mediated allergic reactions are very uncommon and contribute to less than 1% of all LA reactions.^{1,3} Rarely individuals demonstrate hypersensitivity to both ester and amide group LAs.^{2,4} We present the first documented case of ocular bupivacaine desensitization in a patient with suspected ester and amide group hypersensitivity.

A 52-year-old white female with bilateral central retinal vein occlusion and subsequent retinal edema required intraocular ranibizumab injections every 5 weeks with ocular LA pretreatment. In February 2013, the patient began exhibiting reactions to LAs with development of urticaria, throat fullness, dyspnea, confusion, and fatigue within minutes of subconjunctival injection of an amide anesthetic, lidocaine. Subsequent topical conjunctival application of tetracaine and benoxinate, both members of the ester group of LAs, failed as the patient immediately developed shortness of breath, dysphagia, and increased sputum production. Skin prick testing with full-strength benoxinate HCL revealed erythema and a 3-mm wheal. Within minutes of skin testing, she developed tachycardia and urticaria with upper body erythema and was tremulous. She was treated successfully with multiple doses of intramuscular epinephrine, intravenous methylprednisolone, and normal saline fluid. Following these reactions, a challenge with topical bupivacaine and subsequent subconjunctival bupivacaine injections were tolerated. However, after 3 years of repeated bupivacaine treatments, she developed a transient episode of pruritus, dysphagia, and heart palpitations within minutes of an ocular bupivacaine injection. Within 1 hour of the procedure, the patient developed a second reaction composed of chest tightness and shortness of breath responsive to inhaled albuterol.

The patient was reevaluated 2 weeks after this reaction. Baseline serum tryptases and urinary histamine levels at that time were found to be normal. Skin testing was performed to mepivacaine 1%, bupivacaine 0.25%, lidocaine 2%, and prilocaine 4%, all of which were preservative-free. Initial skin prick testing

yielded no reaction for all LAs tested. Intradermal skin testing results at 1:100 dilution were negative with the exception of a 3-mm wheal noted to mepivacaine. Full-strength intradermal testing to the 3 remaining LAs revealed a 3-mm wheal with erythema to lidocaine and a 4-mm wheal with erythema to prilocaine and was negative to bupivacaine.

One of the main complications of central retinal vein occlusion is legal blindness. Because of the morbidity of the disease, it was crucial for the patient to be continued on ranibizumab injections every 5 weeks with LA pretreatment. Because of the patient's history of immediate hypersensitivity reactions to multiple LAs and most recently a suspected immediate and delayed hypersensitivity reaction to previously tolerated bupivacaine, an ocular desensitization protocol was designed (Table I) for bupivacaine in an attempt to allow ranibizumab treatment to proceed. Pretreatment with cetirizine 10 mg orally the evening before and the day of the procedure was used to optimize safety and success of the desensitization. Peripheral intravenous access was obtained before the desensitization.

The desensitization protocol was started by diluting bupivacaine to a concentration of 1:1000 and began administering 0.03 mL topically. Then, every 15 minutes 0.03 mL of an increased concentration of the diluted bupivacaine was given. Five minutes after the fifth application (see Table I), the patient experienced a brief episode of tachycardia to 158 beats per minute without any additional symptoms. This spontaneously resolved without treatment. As a precautionary measure, the patient did receive 1 dose of diphenhydramine (25 mg intravenously) 5 minutes after the tachycardia resolved. The patient completed the desensitization procedure (see Table I) without further difficulty and ultimately tolerated her ranibizumab injection. She has subsequently undergone several more monthly procedures without adversity using the protocol described above. Of note is the fact that the total dose of bupivacaine administered was 3 to 4 mg, well below the usual cardiotoxic threshold of 1 to 2 mg/kg published in the literature.⁵

This is the first documented case of probable ocular desensitization to an LA in a patient with suspected LA hypersensitivity to both ester and amide LAs. Historically, our patient had experienced hypersensitivity reactions to numerous LAs, including bupivacaine, suggestive of an allergic mechanism. Neither prick nor intradermal skin testing fully supported the entire clinical history of multiple LA hypersensitivity reactions in this patient. A topical desensitization protocol was developed that ultimately resulted in our patient being able to safely receive bupivacaine on a repetitive basis. Clinicians may consider this methodology for patients with suspected LA hypersensitivity who require ocular LA injections and for which there are no alternative agents.

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TABLE I. Ocular desensitization protocol for bupivacaine

Dose	Time (min)	Concentration	Volume (mL)	Dose (mg)	Total dose (mg)	Dilution	Route
1	0	5 mg/1000 mL	0.03	0.00015	0.00015	1 to 1000	Topical
2	15	5 mg/100 mL	0.03	0.0015	0.00165	1 to 100	Topical
3	30	5 mg/10 mL	0.03	0.015	0.01665	1 to 10	Topical
4	45	5 mg/1 mL	0.03	0.15	0.16665	1 to 1	Topical
5	60	5 mg/1 mL	0.3	1.5	1.66665	1 to 1	Topical
6	95	5 mg/1 mL	0.03	0.015	1.68165	1 to 1	Injection
7	110	5 mg/1 mL	0.3	1.5	3.18165	1 to 1	Injection

Preparation

1. Dilute bupivacaine 5 mg/1 mL with 0.9% normal saline in 1:10 dilutions.

2. This is completed in a step-wise fashion to create top dilution of 1:1000.

3. Administer doses every 15 min.

Doses 1-5: 0.03 mL dropped topically to the eye.

Dose 6: 0.03 mL (0.015 mg) injected into eye by ophthalmology.

Dose 7: 0.3 mL (1.5 mg) injected into eye by ophthalmology.

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REFERENCES

1. Bhole MV, Manson AL, Seneviratne SL, Misbah SA. IgE-mediated allergy to local anaesthetics: separating fact from perception: a UK perspective. *Br J Anaesth* 2012;108:903-11.
2. Volcheck GW, Mertes PM. Local and general anesthetics immediate hypersensitivity reactions. *Immunol Allergy Clin North Am* 2014;34:525-46.
3. Schatz M. Skin testing and incremental challenge in the evaluation of adverse reactions to local anesthetics. *J Allergy Clin Immunol* 1984;74:606-16.
4. Becker DE, Reed KL. Essentials of local anesthetic pharmacology. *Anesth Prog* 2006;53:98-109.
5. Cox B, Durieux ME, Marcus MA. Toxicity of local anaesthetics. *Best Pract Res Clin Anaesthesiol* 2003;17:111-36.

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