

Delayed-type hypersensitivity (type IV) reactions in dental anesthesia

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ABSTRACT

The recommended methodology of evaluating patients who have presented with reactions to local anesthetics consists of epicutaneous skin testing and serial subcutaneous challenge. However, the role of type IV reactions in this group has been poorly documented. Epicutaneous routine testing and subcutaneous challenge to local anesthetic was performed, as well as patch testing and subcutaneous rechallenge of both at 24 and 48 hours with evaluation up to 72 hours was performed. Three patients presented with a history of localized edema after dental anesthesia. All had negative lidocaine and mepivacaine testing as well as negative lidocaine challenge on evaluation at 1 hour. The first patient, who had previously reacted to EMLA, reacted to both lidocaine and mepivacaine patch testing and challenge, with delayed swelling at 24 and 48 hours after challenge. This patient subsequently tolerated the ester anesthetic chloroprocaine. Two other patients had strong histories of contact dermatitis. Patch testing and challenge with lidocaine was negative, but strong reactions were found to benzocaine on patch testing. Patients undergoing local anesthetic testing should be screened historically for features and risk factors associated with type IV reactions. This should be considered in patients who react to multiple amide anesthetics, who have delayed swelling, or who have a history of severe contact dermatitis. We confirm previous data showing that patients reacting to benzocaine can tolerate lidocaine and that lidocaine-allergic individuals can tolerate ester anesthetics.

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Key words: Allergic contact dermatitis, anesthesia, benzocaine, chloroprocaine, dental, drug hypersensitivity, lidocaine, local anesthetic, mepivacaine, type IV

Reactions after local dental procedures may be triggered by a number of mechanisms. Vasovagal reactions, epinephrine sensitivity, and reactions to other agents such as metabisulfite¹ and guar gum² should be considered. IgE-mediated hypersensitivity to latex³ also is a concern. Immediate hypersensitivity reactions have been reported rarely with local anesthetics.^{4,5} The diagnostic approach typically consists of prick testing followed by subcutaneous challenge with a single agent and observation for up to 2 hours.^{6,7} The role of type IV reactions to local anesthetics has not been stressed.

MATERIALS AND METHODS

Immediate Hypersensitivity Testing

Prick testing was performed using a Greer Dermapik with 1% lidocaine, 3% mepivacaine, and 1% chloroprocaine.⁸

Delayed Hypersensitivity Testing

Serial subcutaneous challenge was performed with 0.1, 0.5, 1, and 2 mL every 15 minutes reaching a

cumulative dose of 3.6 mL of 1% lidocaine, 3% mepivacaine, and 1% chloroprocaine on separate occasions. Patients were evaluated for 1–2 hours and then reevaluated if swelling occurred up to 72 hours.

Standard patch testing with lidocaine 1%, mepivacaine 3%, and benzocaine 20% (Solarcaine, Schering Plough, Kenilworth, NJ) was performed using 10-mm Finn chambers on Scanpor (Allerderm Lab, Phoenix, AZ; Epitest Ltd. Oy, Tuusula, Finland), in addition, testing with a standard panel was performed with the TRUE Test (Allerderm Lab; Mekos Laboratories As, Hillerød, Denmark). Readings were performed at 72 hours. Testing was scored as follows: 3+, spreading, bullous, and ulcerative; 2+, erythema, edema, papules, and vesicles; 1+, nonvesicular, edema, and erythema; doubtful minor papules only or negative.

Patients

Type IV Reaction to Lidocaine. Patient 1 was a 23-year-old woman with a history of perineal swelling after the application of topical medications for yeast infections. She had a long-standing history of morphea that has been treated with intradermal steroid injections preceded by topical EMLA cream (lidocaine 2.5% and prilocaine 2.5%, Astra Zeneca, Wilmington, DE). She developed a reaction from the EMLA cream consistent with contact dermatitis. She also reported that injected local dental anesthetics caused delayed swelling last-

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Table 1 Proposed screening questionnaire

Have you ever been diagnosed with severe contact allergy such as poison ivy or have you had itchy blistering rashes?

Have you used local anesthetics for sunburn, skin disorders, sexual enhancement, vaginal burning, hemorrhoids, or as part of a cosmetic skin procedure?

Have you had frequent local anesthetic shots?

How long after the injection did the swelling begin and how many hours did this last?

Did you have blistering or swelling of the lining of the mouth after the dental procedure?

ing several days. Skin-prick testing and subcutaneous challenge with lidocaine 1% and mepivacaine 3% failed to elicit a reaction up to 2 hours after injection. However, she developed large localized edema to both local anesthetics at the subcutaneous injection sites at 24 hours. Patch testing with the TRUE Test was negative including "caine mix" (a combination of tetracaine, dibucaine, and benzocaine.) However, she did react to patch tests 3+ with both lidocaine 1% and mepivacaine 3%. Prick testing and subcutaneous challenge with 1% chloroprocaine (a *p*-amino benzoic acid ester anesthetic) was negative for immediate and delayed reaction for up to 72 hours. Patch testing also was negative. Based on these results, she has subsequently tolerated chloroprocaine therapeutically.

Type IV Reactions to Benzocaine. Patient 2 was a 24-year-old woman who presented with delayed swelling lasting several days after injection of novocaine at the dentist's office. This localized reaction resulted not only in mucosal swelling but also sloughing of the mucosa near the injection site. She had a history of severe contact dermatitis and had frequently used over-the-counter topical creams containing anesthetics. Prick testing and subcutaneous challenge with lidocaine 1%, mepivacaine 3%, and 1% chloroprocaine was negative. Patch testing with the TRUE Test revealed a 2+ reaction to nickel, paraphenylenediamine, caine mix, and, additionally, to benzocaine 20% at 72 hours. Subcutaneous challenge with 2 mL of 1% lidocaine and 2 mL of 1% chloroprocaine was negative. She subsequently received lidocaine anesthesia in the dental office without additional problems with the suggestion that she avoid all benzocaine preparations in the future. Patient 3 was a 68-year-old retiree with a history of a generalized dermatitis and delayed swelling after local dental anesthesia.

The allergic history was significant with angioedema due to ibuprofen ingestion, latex hypersensitivity, asthma, and allergic rhinitis. Prick testing was negative for lidocaine 1%, mepivacaine 3%, and 1% chloroprocaine. Subcutaneous challenge with lidocaine and chloroprocaine was negative up to 72 hours. Patch testing by the TRUE Test revealed 2+ positive reactions to

mercaptothiobendazole, carba mix, mercapto mix, caine mix, and balsam of Peru. Subsequent testing with 20% benzocaine alone showed a doubtful reaction at 72 hours but a generalized reaction at 96 hours. Subcutaneous challenge with 2 mL of 1% lidocaine and 1% chloroprocaine was negative. She subsequently was treated uneventfully with lidocaine.

DISCUSSION

Type IV reactions to local anesthetics have been reported to only a limited extent in the medical literature.^{5,9} Benzocaine appears to be the most common cause of type IV reactions to local anesthetics,¹⁰ although this may not be true in some countries.¹¹ This topical anesthetic is present in numerous over-the-counter products used for sunburn, vaginal irritation, sexual enhancement, hemorrhoids; tetracaine, another *p*-amino benzoic acid ester, has been associated with type IV reactions in cosmetic as well urological applications.^{12,13}

EMLA crème is a combination of lidocaine 2.5% and prilocaine 2.5%. Type IV reactions to EMLA have been shown to occur because of both agents,^{14,15} and contact urticaria has been described in one patient after EMLA application, which was attributed to the lidocaine component.¹⁶ Kaufman described a patient with a type IV reaction to injected amide anesthetics similar to patient 1 who was initially sensitized to topical lidocaine.¹⁷

Klein¹⁸ described a patient with a delayed reaction to mepivacaine on subcutaneous challenge, with positive patch tests to mepivacaine and as was noted in patient 1, who also reacted to lidocaine on subcutaneous challenge and patch testing. Redfern¹⁹ also described a patient with type IV reactivity to lidocaine, who reacted to other amide anesthetics, *viz.*, bupivacaine and mepivacaine.

Local anesthetics agents classically have been divided into amide and ester groups. An additional subclassification has been proposed dividing up amino-benzoate esters and benzoic acid esters.⁶ Benzocaine and chloroprocaine are ester anesthetics of the *p*-amino benzoic acid ester type. Surprisingly, however, both

patients with benzocaine reactivity tolerated chloroprocaine. This lack of cross-reactivity of benzocaine with other caines has been noted previously¹¹ and therefore would suggest that classification is too simplistic.

The role of prick, subcutaneous challenge, and patch testing provides the clinician with an approach to properly diagnose and manage patients with local anesthetic reactions. Immediate (type I) reactions are rare but type IV reactions should be considered in all patients presenting with reactions after dental anesthesia. In addition to testing, we believe that a simple screening questionnaire as outlined in Table 1 may be useful in identifying these patients.

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