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Review Article

The Usefulness of Skin Prick and Patch Testing for Local Anesthetics in Clinical Practice for Patients with Sulfite Allergy

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Abstract

Patients with a history of confirmed or suspected metabisulfite or sulfite allergy may experience adverse reactions to local anesthetics. Metabisulfites and sulfites constitute the antioxidant addition of local anesthetics. While true allergy to local anesthetics is uncommon, adverse reactions may occur in patients with sensitivities or allergies to sulfites. Determining if a patient is allergic to specific local anesthetics with and without preservatives may be essential in selecting an appropriate anesthetic for clinical practice and patient safety. If hypersensitivity to local anesthetics is suspected, skin testing has been considered a useful tool with both patch and intradermal testing for delayed hypersensitivities and skin prick and intradermal testing for immediate allergic responses. This review paper identifies the clinical practicality, risks /benefits to patients, and appropriate guidelines for local anesthetic allergy skin prick testing for individuals with self-identified allergy to sulfite products.

Keywords: metabisulfites; allergies; anesthetics

Introduction

Adverse reactions to local anesthetics are relatively common, although true IgE-mediated allergy is extremely rare. Patients with suspected allergy to local anesthetics, such as sulfites, should have a detailed history taken, followed by skin testing.

While true allergy to local anesthetics is rare, genuine immunological reactions occur in only about one percent (1%) of all adverse reactions to these medications[1,2]. In the case of suspected true hypersensitivity to local anesthetics, skin tests are considered a useful tool for the diagnosis of sensitization to this group of drugs and for the analysis of cross-reactivity patterns.

Local anesthetic drugs are generally well tolerated, with the rate of adverse drug reactions (ADRs) ranging from 0.5% to 26%[3,4]. The literature on ADRs reported by both patients and providers suggests that ADRs are rarely ever allergic. However, allergic contact dermatitis to local anesthetic drugs are more common than Ige-mediated reactions, and their incidence has been reported to be 2-3%[5,6].

The rarity of reports of Ige-mediated reactions to local anesthetic drugs can be attributed to other causes of ADRs, including:

- Non-allergic causes;
- Additives; or,
- Other perioperative exposures[7].

The subcutaneous challenge (skin prick testing) is considered the “gold standard” for confirming true IgE-mediated allergy to local anesthetics. Negative skin test and subcutaneous challenge with a history of generalized cutaneous symptoms and/or systemic symptoms during the reaction to local anesthetics can be attributed to many causes, such as:

- Ige-mediated reactions against a component other than lidocaine (e.g., sulfites, methylparaben, Latex);
- Medication side-effects (e.g., Adrenalin in combined preparations); and/or,
- Symptoms of primary disease (e.g., chronic spontaneous urticaria/angioedema)[8,9,10].

This article will discuss the utilization of skin prick testing for local anesthetics in clinical practice, in relation to possible or suspected allergic reactions.

Discussion

Sulfites and metabisulfites are chemicals that are used as preservatives to prevent discoloration in foods, beverages, and medications. Sulfite-containing ingredients include sulfur dioxide, potassium metabisulfite, potassium bisulfite, sodium bisulfite, sodium metabisulfite, and sodium sulfite. The use of sulfites as preservatives increased significantly during the 1970s and 1980s, leading to a sulfite ban administered by the Food and Drug Administration (FDA) in 1986 due to the number of severe reactions to sulfites[11]. This ban particularly prohibited sulfite use in fruits and vegetables after numerous allergic reactions to salads in restaurant salad bars raised concern and a need for a change. Sensitivity to sulfites

and metabisulfites can cause asthma and allergy signs or symptoms that range from wheezing and urticaria to life-threatening anaphylactic reactions. When a patient experiences a sulfite allergy, food and medication labels must be checked for sulfites in order to prevent an adverse reaction. Today, sulfites are still used in potatoes, canned vegetables, seafood, wine, and pharmaceutical products. Sulfites are also used as antioxidants in fresh fruit and vegetables to preserve color and appearance[12]. Sulfites continue to be used as a preservative in many medications today, including medications used for local anesthetic administration.

While true immunologic reactions to local anesthetics, such as lidocaine and benzocaine, are still considered rare, adverse reactions are more commonly found to the preservatives, antioxidants, and metabolites that are found as additives to local anesthetics. Specifically, allergies to sodium bisulfite and metabisulfite are not uncommon[13]. Allergic reactions to local anesthetics may be caused by a sensitivity to 1) the amide or ester component 2) methylparaben or 3) antioxidant sulfites[14]. When a patient reports an allergy to any component of the anesthetic mixture, skin testing is recommended for confirmation prior to anesthetic usage[15]. Skin testing allows the clinician to differentiate between autonomic responses from true allergy to local anesthetics. This type of intradermal testing allows for components of the anesthetic solution to be separated and tested separately to localize the source of allergy. Local anesthetics and vasoconstrictors may contain metabisulfite as an antioxidant, both metabisulfite and methylparaben as an antioxidant and preservative, or only methylparaben as a preservative. Due to the different antioxidants and combinations of preservatives that may be found in routine local anesthetic usage, intradermal testing should include methylparaben, metabisulfite, and local anesthetic solutions[15]. If skin testing indicates a true allergy to one or multiple components of the local anesthetic solution, appropriate precautions and measures can be made to ensure the patient does not have an adverse reaction during their procedure. Sulfites are used as additives in local anesthetics to prevent the oxidation of vasoconstrictors, such as epinephrine or levonordefrin[12]. Without sulfites, the vasoconstrictor component would lose its effectiveness before even making it to the syringe from the manufacturer, so they are a component of any local anesthetic with a vasoconstrictor. The vasoconstrictor component is necessary in achieving hemostasis and increasing the duration of anesthetic effects due to a delay in anesthetic absorption. Antioxidants are found in both ester and amide local anesthetics. The ester anesthetics that contain sulfites are procaine and tetracaine. The amide anesthetics containing antioxidants are lidocaine and bupivacaine[14]. The antioxidant most commonly used is sodium metabisulfite. When a patient suspects a sulfite allergy, an evaluation by a physician and allergy testing may be performed in order to confirm a diagnosis and avoid sulfite-containing products. A history of allergic reaction to any previously administered local anesthetic or the components within it should be evaluated by the physician prior to any procedure requiring local anesthetic. Specifically, if a patient reports a moderate to severe adverse reaction to sulfites, metabisulfites, bisulfites, or a previously administered local anesthetic, the clinician should choose to either administer skin prick allergy testing or avoid anesthetic products with which the patient reports allergy. If a certain agent was noted as the culprit of the allergic response, ensure that the alternative anesthetic does not include the same antioxidants and preservatives as the one responsible for the prior allergy.

An allergic reaction to a local anesthetic must not be immediately ruled out as an intravascular injection, toxic overdose, idiosyncratic occurrence, or psychogenic reaction. Confirmed true allergic reactions to components of anesthetics have been documented and most commonly present as type I anaphylactic reactions and type IV delayed hypersensitivity responses. Due to several confounding variables during the administration of local anesthetic (preservative changes, additives, addition of epinephrine, latex, plastics), skin prick testing must be administered on an as-needed basis for prior moderate to severe reactions to any local anesthetic procedure[16]. When there is a suspected allergy to any component of the local anesthetic, patients should be referred for allergy and skin prick testing. Testing offers great benefits in determining which drugs can be administered safely to the patient without adverse outcomes.

In terms of diagnosis, historical literature shows oral challenge tests and FEV and FEV at interval measurements have previously been used when diagnosing sulfite sensitivity[17]. When patients presented in the past with asthma, atopy, and allergic-like symptoms, sulfite oral challenges would be conducted to assess for allergy. Oral challenges are able to use a variety of sulfite products (sodium metabisulfite, SO2) in solution. Due to the severity of ingesting sulfites that one may be allergic to, this type of diagnostic testing has to be performed in a hospital setting. Intradermal patch testing and skin prick testing may also be used to diagnose sulfite sensitivity[18,19]. The validity of patch testing for sulfite sensitivity was performed in a research study, and sensitivity to sulfite was confirmed in 92% of cases[20]. While further research is warranted to compare the diagnostic utility of patch and skin prick testing versus oral challenge testing, patch and skin prick testing are undeniably a safer option to perform in a clinic setting for quick and effective allergy outcomes.

Drug hypersensitivity reactions vary from isolated, benign skin conditions to severe cutaneous adverse reactions. The benign skin conditions usually resolve rapidly with no treatment necessary, drug discontinuation or even with continued drug treatment. Severe cutaneous adverse reactions are the result of lifelong memory T-cell responses can be associated with long-term morbidity and mortality. Diagnostic approaches to delayed hypersensitivity reactions include patch testing, delayed intradermal testing, and drug challenges for milder reactions. Drug patch tests are applied to the upper back, arms, or abdomen on unaffected skin. This is done using chambers that contain the allergen that are secured to the skin with a hypoallergenic tape. These patches are left for 48 hours and then the skin is inspected 48 hours afterwards. Reactions for the allergens are graded on a spectrum ranging from negative to +++ strong reaction[21]. With an intradermal test, the provider injects possible allergens into the epidermis via a small needle. After 15 minutes, any wheals or discolored spots are measured with a ruler. If the skin test is negative for any medication, there is a second intradermal test stage. During the second stage, a stronger solution of the allergen is inserted. After 10 minutes, any reactions are measured again[14]. Immediate allergic reactions are mediated by the IgE class of antibodies. These reactions typically occur 15 to 20 minutes after allergen exposure. IgE binds to mast cells and basophils, which contain histamine granules that are released and cause inflammation during the reaction. Otherwise known as type I hypersensitivity reactions, these can be seen in asthma, allergic rhinitis, allergic dermatitis, food allergy, and anaphylactic shock[22]. Skin prick testing can be used as an initial test for medication allergies and can be followed up with intradermal testing. A lancet is used to prick the skin with a small amount of different possible allergens near an allergen label marker. This is done with a positive control that contains a histamine solution (which causes a wheal) and a negative control that contains a saline solution (causes no wheal). After 15 minutes, any wheals or discolored spots are measured with a ruler[14].

In regard to the patient's care, skin prick allergy testing and patch testing for suspected sulfite allergy prior to local anesthetic administration has far greater benefit than potential harm to the patient. While side effects of skin prick allergy testing and patch testing may include redness, local irritation, pruritus, and inflammation at the site of allergen placement, positive allergy responses will provide the patient with confirmation regarding their suspected allergy. If the allergy to sulfites is confirmed after a self-identified allergy or prior adverse reaction to local anesthetic, the patient will have the knowledge and guidance to avoid certain medications, foods, and preservatives that may have led to future serious adverse reactions or even death by anaphylaxis. Skin prick and patch allergy testing provide a much safer and accessible diagnostic option to oral challenge testing due to rapid availability of use in outpatient clinics and elimination of hospital administration due to concerns of severe anaphylactic response.

Conclusion

For optimal patient care and allergen diagnosis, skin prick and patch testing have utility in diagnosing allergy to sulfites and preservatives found in local anesthetic preparations. The benefits of skin prick and/or patch testing for sulfite allergy outweigh the harm and risk to patients when the patient has a prior documented moderate to severe allergic reaction or hypersensitivity to sulfite in foods or to prior local anesthetic administration. Since skin prick and patch testing have been found in small studies to have a high sensitivity for sulfite allergy and are a much safer alternative to oral challenge testing, cutaneous testing for sulfite allergy proves to be superior in a clinical setting for evaluating true allergy to sulfites or additional local anesthetic additives. In summary, sulfite testing via skin prick or patch testing should be considered as a routine diagnostic tool for diagnosing true sulfite allergy prior to local anesthetic administration when patients have had a previous moderate to severe documented adverse reaction to sulfites or a previous local anesthetic preparation.

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