

Labelling and Delabeling in Local Anesthesia Allergy Patients: Practice perspectives

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Local Anesthetics (LA) are considered the most commonly used drugs in various branches of medicine¹. Even though hypersensitivity to these agents is uncommon, given the widespread and ever-expanding use with medical, surgical and dental-care health facilities reaching places far and wide, adverse reactions to LAs need to be thoroughly examined.

SKIMS Allergy & Immunology clinic being the only centre in the entire region (UTs of J&K & Ladakh) managing drug allergies, patients "labelled as" or "suspected of" hypersensitivity to LAs visit frequently for confirming or ruling out the same. Some of these patients approach directly, while most are referral cases mainly from the different dental-care hospitals/clinics.

True allergy to local anaesthetics is uncommon, with a genuine immunological reaction representing only 1% of all adverse reactions to LAs²⁻⁴. However, once this true reaction occurs in the form of anaphylaxis, it becomes a significant concern because its onset is rapid and may be fatal. In traditional classifications, adverse reactions to LAs have been categorised as allergic, toxic and autonomic². Most of the patients undergoing dental procedures exhibit an autonomic response to injection, such as sweating, tachycardia or even syncope. However, it is usually mild and transient. Toxic reactions are mainly observed due to a rapid intravascular injection of LA or may be associated with an overdose in patients defectively metabolising the drug¹. As far as allergic reactions are concerned, type I and IV allergic responses are involved in most abnormal immune reactions to LAs⁽⁵⁾. Therefore, its nature should be

thoroughly examined whenever an adverse reaction occurs as to whether the event was due to autonomic, toxic or allergic reasons.

Interestingly, allergy to LAs is often readily accepted by the patients who expect this to be proven or ruled out by some easily carried out diagnostic methods which they perceive are readily available. However, it is not that simple. Usually, these patients are often only "suspected" cases of hypersensitivity to LAs, and the previous adverse reaction has taken place several years before the testing. Reliable documentation of the event remains unavailable. Therefore, these patients remain terrified of receiving LAs. To add to the burden, the treating doctor (usually the Dentist) wants to have a clear opinion from the Allergist viz-a-viz the safety of usage of the LAs in these patients.

Proper diagnostic procedures allow the facility to save the patient from a severe life-threatening adverse event in the future. The whole idea is to "delabel" the wrongly labelled local anaesthesia allergy patients with only a suspicion of such drug allergy. These patients remain unnecessarily scared and deprived of receiving local anaesthetics even in times of dire need for the same, thereby leading to their becoming dental "cripples and phobics". On the other hand, if the patient tests positive for the LA on sensitivity testing, i.e., a true allergy to some LA is confirmed, in that case, a similar diagnostic sensitivity test for a safer alternative LA can be carried out to minimise the risk to these patients. The

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ultimate goal is to find a local anaesthetic that can be safely administered to provide the patient with safe and comfortable dental/other treatment.

According to their chemical structure, local anaesthetics have traditionally been divided into two groups: Esters and Amides⁶. Most sensitisation reactions were attributed to the ester anaesthetics. One of the breakdown products of procaine is the highly antigenic agent p-aminobenzoic acid(PABA). As this is a standard breakdown product of many ester anaesthetics, cross-allergenicity is expected. The breakdown products of the local amide anaesthetics do not include a primary amine in the para position as seen with p-aminobenzoic acid (PABA); therefore, this may account for the rarity of sensitisation reactions. Consequently, cross-hypersensitivity among amide anaesthetics or between amide and ester anaesthetics is not seen¹. It is rare in dentistry that ester-type drugs are used for local anaesthesia purposes. However, these anaesthetics are used more commonly for topicalisation before injection to reduce discomfort associated with mucosal needle puncture⁷.

Other causes of allergy are attributed to additives in local anaesthetic preparations: the parabens, which are used as preservatives for the anaesthetic solution, and sodium bisulfite, an antioxidant for the vasoconstrictor. A breakdown product of the parabens is p-aminobenzoic acid; consequently, a patient allergic to ester anaesthetics may also demonstrate an allergic reaction to amide anaesthetics containing this agent. Most single-dose anaesthetic solutions no longer contain parabens. Sulfites are used as preservatives in some foods; therefore, one should avoid administering sulfite-containing local anaesthetics solutions to patients with an extensive history of food allergies where sulfites may be involved^{9,11,16-19}.

Lignocaine (Lidocaine, Xylocaine) is an aminoamide type of local anaesthetic agent. It is probably the most widely used local anaesthetic agent as a topical and injectable anaesthetic and intravenously in treating cardiac arrhythmias. Most reactions of Lidocaine are type 1 immediate hypersensitivity⁸. Therefore, we also test for Lidocaine as the first choice in most patients in our set-up.

Testing patients with suspected allergies to LAs is always carried out under controlled conditions where resuscitative measures remain available. Skin testing is a valuable tool;

patch test and intradermal tests for delayed hypersensitivity and skin prick tests and intradermal tests for immediate reactions. The LA (without preservatives or adrenaline) is skin tested. The following are the steps followed for local anaesthetic allergy testing in a suspected allergy patient.

A. Patient Evaluation

1. A thorough medical history is essential.
 - i. The history should include as much detail as possible about his allergies and drug reactions.

Basic information should include the procedure for which the drug was used, name of the drug, formulation of the drug, the amount administered, the presence of any vasoconstrictor or other additive, any medications taken at the time of reaction, details of the reaction, the position of the patient in the dental chair, and the treatment given^{9,10}. Current medications the patient may be taking cannot be excluded as the cause of the allergic reaction. Thus, for each drug being taken, one should determine the duration of use, the time of the last administered dose, and the probability of the drug as an allergen. Determining which drug caused the allergic reaction may only be accomplished by a careful process of elimination. This history may be complicated to document accurately, even when the patient and the attending doctor (who was present at the time of reaction) are questioned.

- ii. Food allergies should be identified when possible. Food products often contain sulfite preservatives; consequently, their ingestion may elicit an allergic reaction. These individuals are considered high-risk patients^{5,11,12}.
- iii. The patient's past anaesthetic experience(s), including any complications, should be evaluated.
- iv. Current medications and dosages should be listed and confirmed by consultation. Medications interfering with skin testing results like antihistamines, long term corticosteroids, tricyclic antidepressants, etc., need to be stopped for varied periods before testing, depending on the class of such drugs that the patient is on.
- v. Patients on beta-blockers need to stop them 3-7 days before the test.
- vi. An overall clinical review of systems should be carried out to ensure that no such comorbidity exists as may

contraindicate the testing or warrant a clearance or consultation from a co-speciality.

B. Patient Preparation and Management

1. An informed consent form concerning the procedure and risks should be explained and signed, including the possibility of localised tissue damage or systemic response to the anaesthetic agent¹³.
2. The patient and attendants should be taken into confidence, and the testing process should be explained to the patient to allay any anxiety or fear. He must have a good idea of how the test is carried out, and there should be no surprises for him.
3. The patient should be without food or drink for 6 hours before testing to reduce the possibility of aspiration of gastric contents if the patient loses consciousness.
4. Proper measurement of blood pressure, pulse, respiration and electrocardiogram should be employed.
5. An intravenous infusion using a 16- or 18-gauge catheter is begun to provide a route for drug and fluid administration in a reaction.
6. A complete emergency kit including oxygen with positive pressure ventilation capabilities must be readily available.
7. The patient should never be left unattended. Verbal communication and monitoring of vital signs are essential.

C. Injection Procedure

1. Specific injection areas (usually on the forearms) are marked approximately 3 cm apart and prepared by cleansing with a sterile alcohol swab and allowed to dry¹⁴. The arm without the intravenous infusion is used.
2. The test agent should be unknown to the patient at injection time.
3. A prick test is performed for each agent as follows:
 - a. Two-tenths of a millilitre of full strength agent is placed on the cleansed skin.
 - b. A 30-gauge needle is used to superficially "prick" the skin, making sure not to draw blood.
 - c. To ensure standardisation of skin prick testing, histamine is used as a positive control and normal saline as a negative control.

- d. Saline (negative control) is pricked first, followed by LA and histamine at last.
- e. The negative control is interpreted as acceptable if its wheal diameter is <3 mm in diameter. The positive histamine control has to be 3mm in diameter and 3 mm larger than the negative saline control for the test to be considered reliable. A positive skin test is interpreted as ≥ 3 mm larger than the negative saline control. The negative control signifies the baseline reactivity of the skin. A positive histamine control less than 3 mm in diameter suggests interference such as suppression by antihistamines.

f. Interpretation of results:

SPT	Results	Wheal Diameter
	–	Wheal diameter of LA <3mm
	+	Wheal Diameter of LA 3mm greater than that of Negative Control (Saline)

- g. A 20-minute interval is allotted for evaluation before performing the intradermal injections.

4. Intradermal testing:

- a. Local anaesthetic test solutions are prepared by diluting the concentration to the desired dilutions (1:10 and 1:100) with sterile saline.
 - b. The intradermal (intracutaneous) injection is performed by inserting the needle tip, bevel up, just underneath the skin's surface and injecting 0.1 mL of the agent. A "bleb" should be formed if the injection is adequately performed^{14,15}.
5. The injection sequence of test solutions is as follows:
 - a. The 1: 100 dilutions are administered first with a 10-minute interval between injections. They are evaluated as described below and before administering the subsequent dilutions.
 - b. The 1: 10 dilutions are administered next unless precluded by a significantly positive reaction to the 1: 100 dilution. The time intervals between injections are as previously described.
 - c. The full-strength test solutions are administered next unless precluded by a significantly positive reaction to the 1: 10 dilution. The time interval between injections is as previously described.

- d. Evaluation of response: IDT is considered positive if at 10 minutes there occurs an increase of >3 mm in previous bleb size compared to when the intradermal injection was just given²⁰.
- e. If no response occurs to the prior injections, a 1mL subcutaneous injection of full strength anaesthetic is performed on the arm. A tourniquet is placed above the injection site if a response occurs to this injection, and appropriate treatment is rendered.

6. Post-Allergy Test Sequence

- i. The patient should be observed for 1-1.5 hours after the last injection to determine that no delayed reaction will occur and ensure patient safety.
- ii. If a reaction occurs, the patient must be monitored and appropriately treated, then referred for additional medical treatment.
- iii. if the patient tolerates well the full concentration subcutaneous dose also, he is reported as having tested negative for the LA sensitivity testing and is advised to use the LA preparation without preservatives, i.e., the LA solution similar to the one that he was tested with. Most single-use LA solutions contain no preservatives.

Since there is a negligible cross-reactivity viz-a-viz allergic reaction within the amide group of local anaesthetics members, those patients testing positive for Lidocaine on skin testing must be tested for Bupivacaine which is a suitable alternative from the same class of LAs. In case the patient tests positive for Bupivacaine also. The next safer choice of LA would be Diphenhydramine (DPH) 1% injection, an antihistaminic agent that can serve as a local anaesthetic at this concentration²¹. Still, unfortunately, the non-availability of this injection precludes its use. Therefore in these situations, we recommend the option of general anaesthesia for such patients.

In our experience of over 100 patients who presented to us for suspected LA hypersensitivity, more than 90% tested negative for Lidocaine, tolerated it well later and got delabelled from a wrong label of being allergic to LAs. A few patients only who tested positive for Lidocaine successfully underwent a Bupivacaine sensitivity test and received it uneventfully later. As of now, just one patient needed general anaesthesia (GA) after testing positive for Bupivacaine.

Taken all together, the hypersensitivity to LAs is an overdiagnosed phenomenon. Nevertheless, a well-organised drug allergy work-up in such patients can prove highly beneficial. Moreover, safer alternative drugs like DPH must be made available to avoid the risks and inconvenience associated with GA use.

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