Anaphylactic Shock to Lidocaine: A Rare Case With Evaluation of Cross-Reactivity Between Local Anesthetics

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Local anesthetics (LAs) have been widely used to prevent and relieve pain in surgical procedures [1]. Despite the frequent use of these agents, IgE-mediated hypersensitivity reactions (HRs) to LAs are extremely rare (<1%) [1-3].

Most adverse reactions to LAs are not immunologically mediated and are usually associated with procedural trauma, psychomotor responses, or other substances administered concomitantly as additives or preservatives [3,4].

LAs are classified as amides or esters based on their chemical structure. Since the prevalence of true IgE-mediated HRs to LAs is low, little is known about cross-reactivity between these drugs, particularly within the amide group. Case reports have shown various spectrums of tolerance, thus making cross-reactivity patterns more difficult to understand [4-9].

We report the case of a 43-year-old white man with well-controlled NSAIDs-exacerbated respiratory disease who underwent routine nasal endoscopy for monitoring of nasal polyposis. A few minutes after 2 puffs (20 mg) of intranasal lidocaine (Xylocaína Spray), he developed generalized erythema, rhinoconjunctivitis, dyspnea, cough, vomiting, dizziness with hypotension, tachycardia, and hypoxemia. Intramuscular adrenaline was administered, followed by intravenous fluid therapy, clemastine, methylprednisolone, salbutamol, and oxygen therapy. Symptoms improved, with recovery from hypotension and oxygenation. About 1 hour later, hypotension recurred, requiring readministration of adrenaline. The patient's blood pressure improved and stabilized, although atrial fibrillation was documented. He was therefore given digoxin, which reverted atrial fibrillation in a few hours. Serum tryptase was 24 µg/L (basal, 4.9 µg/L). The patient had reported no previous reactions to lidocaine. He was discharged 24 hours later and referred to our drug allergy department.

Skin tests and a basophil activation test (BAT) were performed with lidocaine and all LAs from the amide group available at our center—mepivacaine, articaine, and ropivacaine—in order to assess cross-reactivity.

The formulations of lidocaine (Lidocaine Braun) and ropivacaine (Ropivacaine Krabi) were preservative-free. The formulations of mepivacaine (Scandinibsa) and articaine (Artinibsa) contained preservatives (sodium metabisulphite in both and methylparaben in mepivacaine).

Undiluted formulations for skin prick testing (SPT) and dilutions of 1/10 for intradermal testing (IDT) were used according to European Network of Drug Allergy group recommendations. As the patient had experienced a severe anaphylactic reaction, an intradermal test (IDT) was initially performed with lower concentrations, progressing to the maximum nonirritant concentration (1/1000-1/10). A positive skin prick test (SPT) result was defined as a mean wheal diameter of ≥3 mm compared with the negative control and a positive IDT result as an increment of ≥3 mm compared with the initial wheal. The BAT result was considered positive when activation was >5% and the stimulation index (SI) was >2 in at least 1 concentration.

The results of SPT with lidocaine 10 mg/mL and 20 mg/mL were both positive (8.5 mm and 10 mm) (Figure E1, Online Repository). The SPT result was positive to mepivacaine 30 mg/mL (12 mm) (Figure). SPT and IDT results with articaine and ropivacaine were both negative (articaine, 40 mg/mL for SPT and 0.04-4 mg/mL for IDT; ropivacaine, 2 mg/mL for SPT and 0.2 mg/mL for IDT) (Figure). The BAT result was negative for all the LAs tested (lidocaine, mepivacaine, and articaine).

A placebo-controlled subcutaneous challenge was performed with articaine in the intensive care unit. A 4-step protocol was started with 1/100 of the cumulative dose (40.4 mg), and no reaction occurred. Since the reaction with lidocaine was severe and little is known about cross-reactivity between amide LAs, we decided to perform a rechallenge with articaine using a 2-step protocol 1 week after the first challenge to assess whether the patient had been sensitized during our procedure. No reactions occurred. Drug challenge with ropivacaine was proposed, although the patient refused further investigation.

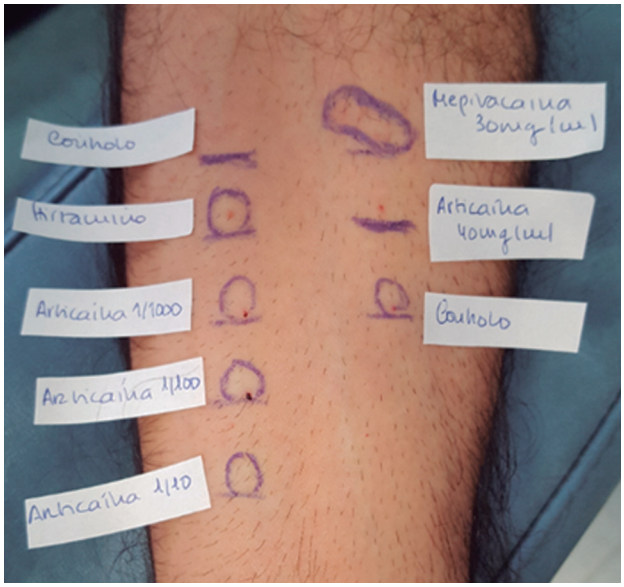

Figure. Results of skin prick testing (SPT) and intradermal testing (IDT) to mepivacaine and articaine.

We report a rare case of severe immediate HR to intranasal lidocaine, with possible cross-reactivity to mepivacaine, but not articaine, which the patient subsequently tolerated. We were not able to confirm tolerance to ropivacaine.

Although the values of IgE to lidocaine and other LAs were not available, the clinical history and diagnostic work-up favors an IgE-mediated mechanism, since the patient experienced anaphylactic shock and the SPT result was positive to lidocaine and mepivacaine.

The diagnostic work-up in patients with suspected HR to LAs is no different from that of other drugs and includes a detailed clinical history, skin tests, and drug challenge [2].

Optimal concentrations for skin tests are well established for LAs, with a negative predictive value reaching 97% [10]. In the present case, skin tests proved useful for establishing a diagnosis of HR to lidocaine and evaluating cross-reactivity between amide LAs, thus enabling safe introduction of an alternative amide LA. Drug challenge is required to confirm HR when skin tests are negative and was essential for confirmation of tolerance to articaine in the case we report. Given that the BAT is not standardized for LAs, inconsistencies between BAT and skin tests may occur.

We would like to highlight that, although some of the LA formulations used had preservatives, HR was ruled out because the lidocaine formulation used to perform skin tests was preservative-free and the mepivacaine and articaine formulations used contained sodium metabisulphite, which was tolerated.

Even though true IgE-mediated HR to LAs is extremely rare, little is known about cross-reactivity between these agents, and the supporting evidence is based on very few case reports [4-9]. If HR is confirmed, tolerance to alternative LAs must be evaluated in order to introduce them safely. As in the case we report, most of the few published cases reports reveal cross-reactivity between lidocaine and mepivacaine [4,5,7,9], and only 1 reveals tolerance [5]. Data regarding cross-reactivity between lidocaine and articaine are even scarcer [7,8].

In conclusion, although extremely rare, immediate HR to LAs with a putative IgE-mediated mechanism can occur. Skin tests are useful in the diagnosis of these reactions and for identifying alternative LAs. The literature shows a variation in cross-reactivity between amide LAs, although additional cases must be reported to better advance our understanding of this phenomenon.

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Conflicts of Interest

The authors declare that they have no conflict of interests.

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