

Cross-Reactivity Among Amide-Type Local Anesthetics in a Case of Allergy to Mepivacaine

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Abstract. Among the various adverse reactions to local anesthetics, IgE-mediated reactions, particularly to the more commonly used amide group, are extremely rare. We report the case of a 39-year-old man who suffered itching and generalized urticaria with facial angioedema 15 minutes after administration of mepivacaine. Skin tests revealed a strong positive reaction to mepivacaine, lidocaine, and ropivacaine, but negative reactions to bupivacaine and levobupivacaine. Furthermore, double-blind placebo-controlled subcutaneous challenge with bupivacaine and levobupivacaine was well tolerated.

We conclude that an extensive allergologic study must be carried out in rare cases of true allergic reaction to amide-type local anesthetics in order to rule out cross reactivity.

Key words: Local anesthetics. Amide group. Allergy. Mepivacaine. Lidocaine. Ropivacaine. Bupivacaine. Levobupivacaine.

Resumen. Las reacciones de carácter IgE mediado a los anestésicos locales, especialmente a los del grupo amida, que son los más utilizados, son extremadamente infrecuentes. Se notificó un paciente de 39 años que presentó prurito y urticaria generalizada a los 10 minutos de recibir mepivacaína subcutánea. Los test cutáneos con mepivacaína fueron claramente positivos, así como con lidocaína y ropivacaína. Los test cutáneos con bupivacaína y levobupivacaína fueron negativos. El test de provocación controlada doble ciego con bupivacaína y levobupivacaína fue bien tolerado.

Podemos concluir que en el caso infrecuente de sensibilización a anestésicos locales del grupo amida, antes de prescribir otro fármaco del mismo grupo, es conveniente realizar un estudio alergológico completo para descartar la existencia de reacción cruzada.

Palabras clave: Anestésicos locales. Grupo amida. Alergia. Mepivacaína. Lidocaína. Ropivacaína. Bupivacaína. Levobupivacaína.

Introduction

A variety of complications associated with procedures involving local anesthesia have been described. Most are thought to involve toxic effects or be related to the surgical procedure requiring local anesthesia. Today there is good evidence in the literature that IgE-mediated reactions to pure local anesthetics, particularly to the more commonly used amide group, are extremely rare [1].

Case Description

A 39-year-old man attended our Allergy Unit for evaluation of an adverse reaction to local anesthetics. The patient reported an episode of itching and generalized urticaria that took place 15 minutes after administration of mepivacaine (Scandinibsa, Inibsa, Barcelona, Spain) 3 months earlier during a nevus extirpation. No other drugs were administered during the procedure. The

urticaria was resolved in a few hours following treatment with oral corticosteroids and antihistamines. Povidone-iodine was used as a local antiseptic during the surgical procedure but the patient tolerated the antiseptic after this episode.

The patient had not undergone local anesthesia since the episode. He had no personal or family history of allergy. The complete blood count and biochemical profile were within the normal range. Total serum IgE was 51 kU/L. The results of a skin prick test were negative for a battery of standard aeroallergens, foods, latex, and *Anisakis simplex*. Prick and intradermal tests with chlorhexidine and Betadine were also negative.

Prick test with 1% mepivacaine (Scandinibsa) was positive (5 mm). In response to an intradermal test with a 1:100 dilution of the anesthetic, the patient developed a 12 × 15 mm wheal with pseudopodia and immediately displayed an urticarial reaction that spread along the forearm and thorax. The reaction subsided within an hour following treatment with antihistamines.

To assess cross-reactivity between different local anesthetics, skin tests were carried out with commercial anesthetics belonging to the amide group. The following drugs were used, free of excipients: 5% lidocaine (Braun, Barcelona, Spain), 0.5% bupivacaine (Braun), 0.25% levobupivacaine (Abbott Laboratories, Queenborough, Kent, United Kingdom), and 0.2% ropivacaine (Astra Zeneca, Sodertälje, Sweden). Prick tests were performed with an undiluted solution of the commercial drug and intradermal tests with a 1:100 dilution. Positive skin test results were obtained for lidocaine (prick test, 5 × 4 mm; intradermal test, 20 × 30 mm wheal associated with an immediate local urticarial reaction) and ropivacaine (prick test, 4 × 3 mm; intradermal test, 10 × 8 mm). Skin tests with bupivacaine and levobupivacaine were negative.

We carried out double-blind, placebo controlled subcutaneous challenge with the local anesthetics that did not elicit a positive response in the skin tests. Both bupivacaine and levobupivacaine were well-tolerated at doses of up to 2 mL of the undiluted anesthetic. For ethical reasons, challenge tests were not carried out with anesthetics that showed a positive result in skin tests.

Discussion

Local anesthetics are widely used in dentistry, minor surgery, and obstetric procedures. The most common complications involve vasovagal or toxic effects, anxiety reactions, and side effects caused by the inclusion of epinephrine with the local anesthetic [2].

Local anesthetics can be classified as ester type—benzocaine, chlorprocaine, cocaine, piperocaine, procaine, tetracaine, etc—or amide type—lidocaine, mepivacaine, bupivacaine, prilocaine, articaine, ropivacaine, etc. Type IV hypersensitivity reactions to local anesthetics have been well documented in the literature, predominantly to ester-type anesthetics [3] but

also to amide type [4]. Local anesthetic-induced contact dermatitis and patch testing commonly reveal cross-reactivity between benzoic acid esters but an absence of cross-reactivity with amide-type local anesthetics.

True immediate IgE-mediated allergic reactions to amide-type local anesthetics are considered a very rare event, as indicated by a comment made by Patterson [5] in 1996 that “In more than 30 years practice in the north west of the United States, there has never been verified an immediate allergic reaction using our diagnostic methodology.” Moreover, cross-reactivity between different amide-type anesthetics has been considered non-existent [6]. Additional data on the lack of IgE-mediated allergy to pure amide local anesthetics has been provided by Berkun et al [7].

Although some reports have documented immediate type I hypersensitivity reactions to amide-type local anesthetics [8-10], little is known about cross-reactivity among these drugs. In some rare cases of allergic reaction to lidocaine mepivacaine and ropivacaine were nevertheless tolerated [2]. Prieto et al [9] reported a patient who reacted to mepivacaine, showed a positive reaction in skin tests with mepivacaine and ropivacaine, but tolerated lidocaine and bupivacaine. Morais et al [10] reported a patient who showed extensive local urticaria after local lidocaine and for whom positive results were obtained in skin tests with lidocaine, bupivacaine, mepivacaine, and ropivacaine.

Our patient presented an immediate hypersensitivity reaction to mepivacaine and cross-reactivity was observed with lidocaine and ropivacaine, but he tolerated bupivacaine and levobupivacaine. We conclude that in cases of true allergic reaction to amide-type local anesthetics, an extensive allergologic study must be carried out before prescribing other local anesthetics of the same type, as cross reaction can occur between them and the pattern of cross-reactivity may vary in different patients. In the case presented here, skin tests were a useful tool for the diagnosis of sensitization to amide-type local anesthetics.

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