

Letter to the Editor

IgE-mediated reaction to mepivacaine

To the Editor:

In August 2006, a 31-year-old woman received 2 cartridges (each cartridge, 66 mg in 2.2 mL) of mepivacaine (Scandonest, Septodont, Emu Plains, Australia) 3% for the relief of dental pain before a procedure. She also had exposure to lidocaine gel and latex gloves. Within a few minutes, she experienced intense pruritus of the hands and feet accompanied by nausea and a need to go to the toilet. She rested for about 10 minutes but then attempted to walk to the toilet, vomited, and had a brief loss of consciousness. Erythema and swelling of the hands was noticed. She was taken to the hospital and treated with parenteral and oral antihistamines but not adrenaline. The patient had no history of allergy to medications or foods and no personal or family history of atopy. Her serum total IgE level was 178 KU/L, and results of allergen-specific IgE tests to latex were negative (ImmunoCAP, Phadia AB, Uppsala, Sweden). She had known previous exposure to lidocaine, but it is not known whether she had previous exposure to mepivacaine. We carried out intradermal skin testing before planned challenge, and the results are shown in Table I. Subsequently, the patient underwent a graded-dose challenge by means of subcutaneous injection of prilocaine 0.5% up to a maximum dose of 2 mL without any reaction and has had further dental procedures with this anesthetic.

An IgE-mediated mechanism was further supported by a positive *in vitro* test result for specific IgE against mepivacaine. The patient's serum showed a level of 1.4 kU_A/L by using an experimental mepivacaine ImmunoCAP (a result ≥ 0.35 kU_A/L was considered positive). In ImmunoCAP inhibition experiments, *in vitro* cross-reactivity between various local anesthetic (LA) drugs was demonstrated (Fig 1). Mepivacaine induced the strongest inhibition of IgE binding, followed by bupivacaine, lidocaine, and prilocaine, respectively. Inhibition correlated well with the intradermal test results and seemed to correlate with the structural similarity between mepivacaine and the other LAs. Thus bupivacaine, which is structurally close to mepivacaine, showed an inhibition almost as good as that of mepivacaine, whereas prilocaine, with a secondary amine function, proved to have a considerably less efficient inhibition. The significantly weaker inhibition with prilocaine is of clinical relevance because the patient, as mentioned, tolerated this LA well.

Large case series of patients tested for adverse reactions after administration of LA agents have failed to identify true allergy,¹⁻⁴ leading to some skepticism that it indeed exists.^{4,5} However, case reports continue to appear of adverse reactions to various LAs that have the characteristics of IgE-mediated allergy and are supported by skin tests.⁶⁻⁹ A few previous attempts to detect specific IgE to different LAs by means of *in vitro* methods were unsuccessful,⁹ and specific IgE (to lidocaine) has previously been reported only once.⁷ In this latter study, no inhibition study was done to prove the specificity of the IgE binding.

This is the first report of a case of mepivacaine anaphylaxis with a confirmed IgE-mediated mechanism.

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TABLE I. Results of intradermal testing

Anesthetic agent	1:100 dilution	Result	1:10 dilution	Result
Mepivacaine	12 mm	Positive	ND	
Bupivacaine	12 mm	Positive	ND	
Lidocaine	8 mm	Borderline	12 mm	Positive
Prilocaine	0 mm	Negative	ND	

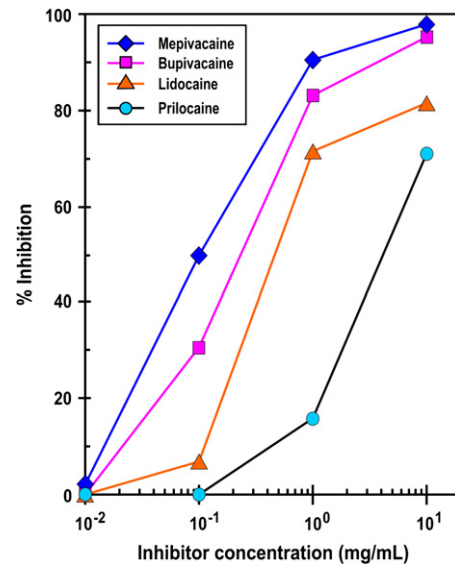


FIG 1. ImmunoCAP inhibition curves. The binding of IgE from the patient serum to the mepivacaine ImmunoCAP was inhibited by mepivacaine, bupivacaine, lidocaine, and prilocaine.

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Disclosure of potential conflict of interest: L. Venemalm is employed by Phadia. F. Degerbeck is employed by Mälarinvest AB. W. Smith has declared that he has no conflict of interest.

REFERENCES

- Gall H, Kaufmann R, Kalveram CM. Adverse reactions to local anesthetics: analysis of 197 cases. *J Allergy Clin Immunol* 1996;97:933-7.
- Chandler MJ, Grammer LC, Patterson R. Provocative challenge with local anesthetics in patients with a prior history of reaction. *J Allergy Clin Immunol* 1987; 79:883-6.
- Berkun Y, Ben-Zvi A, Levy Y, Galili D, Shalit M. Evaluation of adverse reactions to local anesthetics: experience with 236 patients. *Ann Allergy Asthma Immunol* 2003; 91:342-5.
- deShazo RD, Nelson HS. An approach to the patient with a history of local anesthetic hypersensitivity: experience with 90 patients. *J Allergy Clin Immunol* 1979; 63:387-94.
- Baluga JC. Allergy to local anesthetics in dentistry. Myth or reality? *Rev Alerg Mex* 2003;50:176-81.
- Prieto A, Herrero T, Rubio M, Tornero P, Baeza ML, Velloso A, et al. Urticaria due to mepivacaine with tolerance to lidocaine and bupivacaine. *Allergy* 2005;60:261-2.

7. Noormalin A, Shahnaz M, Rosmilah M, Mujahid SH, Gendeh BS. IgE-mediated hypersensitivity reaction to lignocaine—a case report. *Trop Biomed* 2005;22:179-83.
8. Gonzalez-Delgado P, Anton R, Soriano V, Zapater P, Niveiro E. Cross-reactivity among amide-type local anesthetics in a case of allergy to mepivacaine. *J Investig Allergol Clin Immunol* 2006;16:311-3.
9. Cuesta-Herranz J, de las Heras M, Fernandez M, Lluch M, Figueredo E, Umpierrez A, et al. Allergic reaction caused by local anesthetic agents belonging to the amide group. *J Allergy Clin Immunol* 1997;99:427-8.

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