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Inconsistent intracutaneous and patch test results in a patient allergic to mepivacaine and prilocaine

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Case Report

The right wrist of a 48-year-old woman was operated on for carpal tunnel syndrome, using infiltration analgesia with both Carbocain® (10 mg/ml mepivacaine; Suomen Astra, Kirkkonummi, Finland), and Lidocain® (10 mg/

ml lidocaine; Orion Corporation, Espoo, Finland). The skin was sterilized with Klorhexol® (chlorhexidine gluconate). That same evening, the wound area and fingerwebs of her right hand started to itch. The next day, the whole hand was swollen and a vesicular eczema developed on the right hand and the wound. Her surgeon

Table 1. The patient's patch test and delayed i.c. test reactions with local anesthetics

Substance tested	Generic name	Additives	Source	Concentration of anesthetic or allergen (%)	1st. patch test session	2nd. test session; patch tests	2nd. test session; intracutaneous tests
procaine	procaine hydrochloride	no*	C	1	–	NT	NT
aine-mix 3	benzocaine + dibucaine** + amethocaine***	no*	C	10	–	NT	NT
dibucaine	dibucaine hydrochloride	no*	C	1	–	NT	NT
dibucaine	dibucaine hydrochloride	no*	C	5	NT	–	NT
Lidocain®	lidocaine	MPHB	Orion	1	–	NT	NT
lidocaine	lidocaine	no*	C	5	NT	–	NT
lidocaine	lidocaine	no*	T	15	–	NT	NT
hydrochloride							
Xylocain®	lidocaine	MPHB	Astra	2	NT	–	–
EMLA cream®	lidocaine+prilocaine	no	Astra	2.5+2.5	–	NT	NT
prilocaine	prilocaine hydrochloride	no*	C	5	NT	–	NT
Citanest®	prilocaine hydrochloride	MPHB	Astra	1	NT	–	++
tetracaine	tetracaine hydrochloride	no*	C	5	NT	–	NT
amylocaine	amylocaine hydrochloride	no*	C	5	NT	–	NT
Carbocain®	mepivacaine	MPHB	Astra	1	++	–	++
Carbocain®	mepivacaine	MPHB	Astra	0.32; 0.1; 0.032, 0.01	–	NT	NT
Carbocain®	mepivacaine	MPHB	Astra	2; 1; 0.5, 0.25, 0.125, 0.1	NT	–	NT
Marcaïn®	bupivacaine hydrochloride	sodium chloride, sodium hydroxide	Astra	0.75	NT	–	–
Naropin®	ropivacaine hydrochloride		Astra	1	NT	–	–
Klorhexol®	chlorhexidine gluconate	no*	O	0.5	–	NT	NT
paraben mix	MPHB and other parabens	no*	C	12	–	NT	NT

Source: C=Chemotechnique; T=Trolab; O=prepared at the Finnish Institute of Occupational Health.

MPHB: methylparahydroxybenzoate. NT: not tested.

*in petrolatum. **dibucaine=cincaïne (cinchocaine). ***amethocaine=tetracaine.

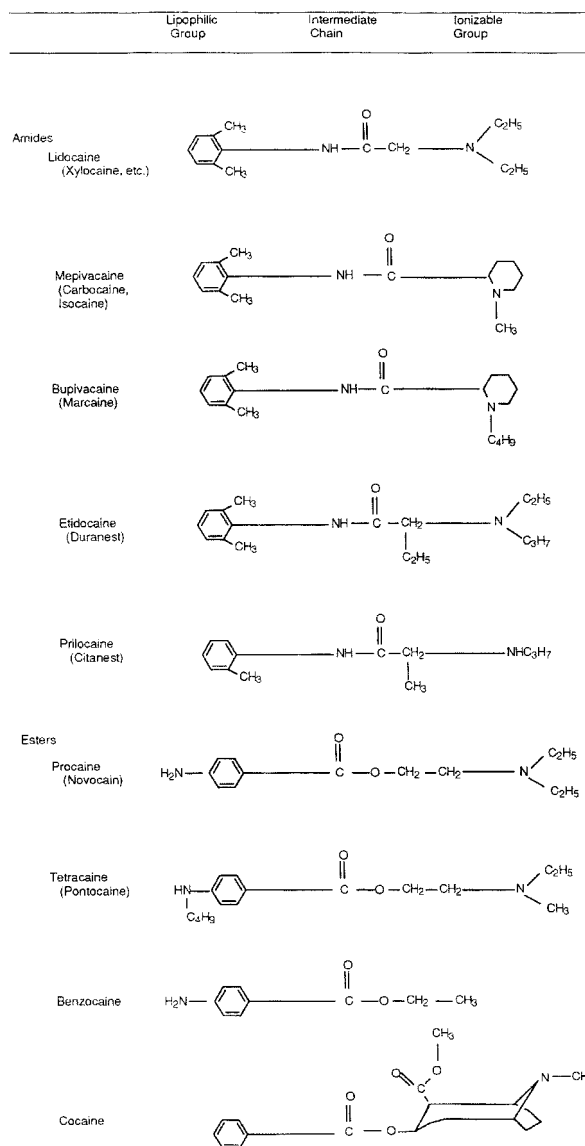


Fig. 1. Chemical structures of local amide and ester anesthetics.

prescribed oral antibiotics and topical corticosteroids. The reaction slowly cleared in 4 weeks.

She was patch tested on the upper back using 2-day occlusion with the Finn Chambers® (1, 2). Scoring was performed according to the guidelines of the ICDRG on readings made on days (D) 2, 3 and 6. Patch tests comprised an antimicrobials series (including chlorhexidine gluconate; Chemotechnique Diagnostics, Malmö, Sweden), commercial local infiltration anesthetics, and local anesthetics of Chemotechnique and Trolab (Hermal, Reinbeck/Hamburg, Germany) in pet. (Table 1). It was shown that the patient had become sensitized to mepivacaine. She was also prick tested with chlorhexidine gluconate (1% aq.) with negative results.

A 2nd patch test session, complemented with intracutaneous (i.c.) tests, was performed 6 months later. I.c. tests with local anesthetics were made by injecting 0.1 ml of anesthetic i.c. and reading after 30 min, and 2, 3

and 6 days. No immediate reactions were observed. The patient's delayed mepivacaine allergy was confirmed by the i.c. test (++) on D2 and D3; negative on D6), whereas the repeat patch test with mepivacaine was negative (Table 1). In the 1st patch test session, EMLA cream containing 2.5% lidocaine and 2.5% prilocaine was negative, whereas i.c. prilocaine hydrochloride (Citanest, Astra) elicited an allergic patch test reaction (on D2 and D3) at 1% in the 2nd patch test session (Table 1).

Discussion

Based on the history and patch test results, the patient had developed a delayed allergy to mepivacaine. Lidocaine did not cause allergic test reactions. The patient had previously undergone local infiltration anesthesia more than 20× for dental or joint treatments. She had a tendency to develop contact allergy, and we have previously reported her (meth)acrylate allergy (1), with allergic patch test reactions as follows: nickel sulfate (+++), cobalt chloride (+++), potassium dichromate (++), palladium chloride (++), para-phenylenediamine dihydrochloride (++), epoxy resin (+++), p-tert. butylphenolformaldehyde resin (++), mercury chloride (++) and diaminodiphenylmethane (++). She also had reactions to several formaldehyde releasers.

Local anesthetics are divided into 2 main classes based on chemical structure: amides and esters (Fig. 1). Allergies to local anesthetics used to be more common when the ester group, e.g., benzocaine, was widely used. The esters include procaine hydrochloride (Novocain®), chlorprocaine hydrochloride (Nesacaine®), cocaine hydrochloride, benzocaine, piperocaine and tetracaine hydrochloride (Pontocaine®, amethocaine). The amides include lidocaine (Xylocaine®), Lignocaine®, bupivacaine hydrochloride (Marcaine®, Bicain®), mepivacaine (Carbocaine®), etidocaine hydrochloride (Duranest®), dibucaine (Cinchocaine®) and prilocaine hydrochloride (Citanest®). Cross-reactions may occur between structurally-related anesthetics, but probably not between esters and amides (2). Because allergy to amides has only seldom been verified, the cross-reaction pattern between amide anesthetics is not well-known. Beck & Holden (3) have suggested that a "caine" mix should preferably be used in the standard series, because it detects many more cases of allergic contact dermatitis than does benzocaine. The caine mix III of Chemotechnique includes the esters benzocaine and amethocaine (tetracaine), and dibucaine (cincaïne, cinchocaine), which contains both an ester (4) and an amide group (5). Our patient was negative on patch testing with caine mix III (Table 1).

Contact allergy to amide anesthetics is rare. According to Klein & Gall (5) in 1991, only 18 cases had been reported since these anesthetics began to be used in the 1940s. There are case reports of delayed mepivacaine allergy (4-9). Mepivacaine has also caused immediate reactions (10) and fixed drug eruption (11). Fregert et al. (4) reported 2 cases of allergy to lidocaine: both patients also reacted to mepivacaine. Curley et al. (7) had a patient sensitized to lidocaine who on patch testing also

reacted to mepivacaine and prilocaine. Bircher et al. (9) had a lidocaine-allergic patient with cross-reactivity to mepivacaine, bupivacaine, and prilocaine, but not to articaine. Cuesta-Herrenz et al. (10) had a patient who reacted to an unknown anesthetic. Prick tests were negative but i.c. tests gave immediate allergic reactions to mepivacaine, lidocaine and bupivacaine. Our patient's allergic test reaction to prilocaine may represent cross-allergy, but there are no clear rules as regards cross-reactivity between various amide anesthetics (2). It is therefore safest to test as many amide-type anesthetics as possible in the case of delayed-type allergy to any member of this family. The commercial patch test substances caine mix III, benzocaine and procaine do not necessarily detect delayed allergy to amide anesthetics, as in our case. Considering its wide use, the sensitizing potential of mepivacaine seems to be low.

Several publications discuss recommendations for patients with local anesthetic allergy (12). Patch testing is the main diagnostic tool, but intradermal (i.d.) tests may be needed in cases of low-grade sensitivity. It has been suggested that an i.d. test needs to be performed because a patch test does not detect immediate allergy, which may result in anaphylactic shock. Our case indicated that i.c. tests may also be needed to detect delayed allergy. Whoever does such testing must be prepared to cope with all possible reactions including anaphylaxis. It is suggested that the same commercial agent used for local anesthesia should be used for allergy testing, especially when testing for immediate allergy. Commercial patch test substances may be of no help, as in our case. Our case indicates that combined patch and i.c. tests may also be necessary to detect delayed allergy to local anesthetics.

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