

ALLERGY Net

ALLERGY 2007 DOI: 10.1111/j.1398-9995.2007.01468.x • © 2007 THE AUTHORS • JOURNAL COMPILATION © 2007 BLACKWELL MUNKSGAARD

• CONTRIBUTIONS TO THIS SECTION WILL NOT UNDERGO PEER REVIEW, BUT WILL BE REVIEWED BY THE ASSOCIATE EDITORS •

Delayed-type hypersensitivity to bupivacaine

E. Nettis*, M. C. Colanardi, G. F. Calogiuri, C. Foti, M. G. Priore, A. Ferrannini, A. Vacca

Key words: bupivacaine; delayed-type hypersensitivity; local anesthetic.

Local anesthetics are classified according to their chemical structure. The two main groups are the 'ester type anesthetics' which are

all derivatives of para-amino benzoic acid (i.e. benzocaine) and the 'amides' which in-

clude the amino acylamides (lidocaine, mepivacaine), amino alkylamides (i.e. procainamide) and the quinoline derivative dibucaine. Delayed allergy to local anesthetics of the ester type such as tetracaine has previously been reported (1). So far, there have been few reports of type IV hypersensitivity to 'amides' (2), in particular bupivacaine. We present a patient who developed an eczematous reaction after continuous epidural analgesia with bupivacaine 0.075% infusion.

The patient was a 33-year-old woman with no history of atopy, parturient at 39-week gestation. During the active phase of labor, to relieve the pain and allow a comfortable delivery, the patient underwent continuous epidural analgesia, after giving informed consent. The epidural administration technique consisted of placing the catheter in the L3–4 interspace under sterile conditions. Then, a loading dose of bupivacaine 0.075% was administered to ensure a diminished

pin-prick sensation caudal to the T10 dermatome. The epidural infusion continued up to delivery, that occurred without any complications. About 3 days later, the patient developed an itchy, vesicular, eczematous reaction on the back and trunk up to the neckline. She was treated with topical steroids and the lesions disappeared within 10 days. About 4 months afterwards, on completion resolution of the lesions, the patient was referred to the Allergy Clinic of Bari University Hospital, where, in view of her history, we decided to perform cutaneous tests.

The patient was patch tested to a rubber additive series, to natural rubber latex, to the SIDAPA (Società Italiana di Dermatologia e Allergologia Professionale e Ambientale) standard series and bupivacaine (0.5% aq). Patch testing was conducted with Finn Chambers® (Epi-test, Tuusula, Finland), which were applied on the back using Scanpor® tape (Norgesplaster, Vennessla, Norway) and removed after 2 days. Readings were made at day (D) 2 and D4. Reactions were evaluated according to International Contact Dermatitis Research Group recommendations (3). Doubtful or irritant reactions were considered negative. On completion of readings on D4, each positive result was assessed in relation to the patient's occupation and clinical history. To carry out the latex patch test, a commercial nonammoniated latex (Chemotechnique Diagnostics AB, Malmö, Sweden) was applied using IQ chambers. A positive reaction was observed only to bupivacaine (+ + +), while all the other patch tests were negative.

To find an alternative local anesthetic to be administered when necessary, we performed an Incremental Challenge Test (ICT) with mepivacaine free of adrenal-ine and preservatives (Carbocaina 3%, 2 ml vials; Astra farmaceutici, Milan, Italy) (4). The test was started with an undiluted drug prick test; then, because

the finding was negative, an intradermal test followed after 15 min, with the drug diluted 1/100; because this was negative too, the subject received s.c. administrations at 15-min intervals of 0.1 ml of a 1/10-dilution and 0.1, 1, and 2 ml of undiluted drug. However, 2 days after the test, eczematous reactions, with erythema and papules, appeared on the patient's arms where the test had been performed. Hence, about 15 days after, we performed ICT with articaine (Citicartin 1 : 200 000, 1.7 ml vials; Molteni dental, Florence, Italy), as described above. The drug was tolerated and no reaction appeared either at the time of testing or during the following days.

Based on these results, the patient was advised to inform physicians that only articaine could be administered to her as a local anesthetic. This is the first report of a delayed hypersensitive reaction to bupivacaine. To find a replacement local anesthetic for the patient, we chose to test mepivacaine, as the patient had used this drug previously during dental procedures (information requested and given by her dentist), up to 2 years before the adverse reaction, without any problems. In addition, as reported by other authors, there is no cross reactivity (referred to type IV hypersensitivity) between mepivacaine and bupivacaine (5). Unfortunately, in our case, the patient did react to mepivacaine, although the reaction was delayed; the type of reaction was the same as those that appeared after the use of bupivacaine, showing the same mechanisms. In this case, the sensitization to bupivacaine is most likely the expression of cross-reactivity with mepivacaine (in fact, there was no evidence that bupivacaine had ever been used in this patient).

On the basis of this result, we decided to test articaine that is an amide, but has a substitute thiophen ring, whereas all amino acylamides have a methylated phenyl ring. This difference may explain the lack of cross reactivity of articaine. With this report we wish to warn of the

possibility of a delayed hypersensitive reaction to bupivacaine. If this occurs, a valid local anesthetic to be used as an alternative is articaine (nevertheless, to be administered only after previous ICT).

*Cattedra di Allergologia e Immunologia
Clinica

Padiglione Chini – Policlinico

Piazza Giulio Cesare

70124 Bari

Italy

Tel: 0039 080 5592821

Fax: 0039 080 5478780

E-mail: e.nettis@allergy.uniba.it

Accepted for publication 26 May 2007

Allergy 2007

© 2007 The Authors

Journal compilation © 2007 Blackwell

Munksgaard

DOI: 10.1111/j.1398-9995.2007.01468.x

References

1. Fernandez-Redondo V, Leon A, Santago T. Allergic dermatitis from local anesthetic on peristomal skin. *Contact dermatitis* 2001;**5**:358.
2. Klein CE, Gall H. Type IV allergy to amide-type local anesthetics. *Contact Dermatitis* 1991;**25**:45–48.

3. Wilkinson DS, Fregert S, Magnasson B, Bandmann HJ, Calnan CD, Cronin E et al. Terminology of contact dermatitis. *Acta Derm Venereol (Stockh)* 1970;**50**:287–292.
4. Nettis E, Napoli G, Ferrannini A, Tursi A. The incremental challenge test in the diagnosis of adverse reactions to local anesthetics. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2001;**91**:402–405.
5. Prieto A, Herrero M, Rubio M, Tomero P, Baeza ML, Velloso A et al. Urticaria to mepivacaine with tolerance to lidocaine and bupivacaine. *Allergy* 2005;**60**:261–262.