

Systemic allergic contact dermatitis from intravenous piritramide

K. Waltermann, J. Geier¹, P. Diessenbacher, D. Schadendorf, U. Hillen*

Keywords: allergy; contact dermatitis; opioid analgesics; piritramide.

A 51-year-old woman received treatment with Dipidolor® (Janssen-Cilag GmbH, Neuss, Germany) (piritramide, intravenously administered), diclofenac and paracetamol for postoperative pain after surgery of a herniated vertebral disc in 2004.

Two days later, she developed a generalized intensively itching erythema. Further postoperative medication was

ambroxol and omeprazole. As intolerance to the analgesics was suspected, piritramide, diclofenac and paracetamol were withdrawn and a treatment with oral corticosteroids (prednisone, 100 mg/day initially with tapering off after 7 days) was started. Under this therapy, skin eruption resolved hesitantly over a period of about 14 days.

The patient's history revealed that piritramide had been administered three times before as postoperative analgetic treatment: first in 1994 without any side-effects and thereafter in 2001 and in 2002, each time causing postoperative pruritus with increasing intensity, but without erythema. In 2006, another

vertebral operation was performed without application of piritramide, but with administration of nonsteroidal antiphlogistics. No skin eruptions were observed at this time.

The patient now presented in our department needing therapeutic options of strong analgesics because of a planned vertebral surgery. Considering the history and the anaesthesiologists' requests, we performed skin prick, scratch and patch tests with Dipidolor® injectable solution (piritramide, tartaric acid, water for injection, tested as is), Tramal® drops (Grünenthal GmbH, Aachen, Germany) (tramadol, tested as is), Tilidin comp® drops (Hexal AG, Holzkirchen, Germany) (tilidine + naloxone, tested as is) and Temgesic® sublingual tablets (buprenorphine, tested soluted in NaCl). Patch test to Dipidolor® (piritramide) was positive after 72 h. Skin tests of the other analgesics were negative. Subsequently, oral challenge tests with Tramal®, Tilidin comp® and Temgesic® (Essex Pharma, Munich, Germany) with cumulative doses in the range of standard daily doses were performed and well tolerated.

Cutaneous side-effects from opioid analgesics are well known. Urticaria, flush and pruritus are often found because of nonimmunological histamine release triggered by many opioids (1). But also delayed-type hypersensitivity reactions have been described, with Codeine being the most frequently reported allergen (2, 3). In addition, there are some reports on occupational allergic contact dermatitis to morphine and its derivatives, including heroin (diacetylmorphine), in workers of the morphine industry (in the beginning of the last century) and medical staff (4). Cross-reactivity between codeine,

morphine and heroin observed in patch tests was frequently mentioned in these reports (3, 4). The most probable reason is the similar chemical structure of these substances, all belonging to the same chemical group of opioids (derivates of morphine). No cross-reactions were seen to chemically unrelated opioids such as fentanyl or tramadol (3, 4).

About 10 years ago, buprenorphine and fentanyl containing transdermal delivery systems were introduced. In the last 4 years, allergic contact dermatitis to transdermal buprenorphine was reported, whereas contact allergy to transdermal fentanyl, chemically unrelated to buprenorphine, was not observed (5).

To our knowledge, this is the first report on a piritramide-induced systemic contact dermatitis. Further ingredients of Dipidolor®, i.e. tartaric acid and water for injection, seem to be very unlikely as cause for the skin reaction.

In the database of the Information Network of Departments of Dermatology (IVDK), an epidemiological surveillance system on contact allergy with 50 Departments of Dermatology from Germany, Austria and Switzerland participating (6) and currently comprising data of more than 165 000 patients, patch tests with Dipidolor® are registered in 43 patients with no unequivocal positive test reaction. In the literature, only one doubtful reaction on piritramide is reported in one of 28 medical staff members, tested in the context of a suspected contact allergy to heroin (4).

Piritramide belongs to the opioids of the methadone group. We found no cross-reactions to tramadol, tilidine and buprenorphine, all structurally unrelated to piritramide, and the tolerance of these opioids was confirmed by oral challenge tests.

We report on the first case of a piritramide-induced systemic allergic contact dermatitis.

*Department of Dermatology
University Hospital of Essen
University of Duisburg-Essen
Hufelandstr. 55
45147 Essen
Germany
Tel.: +49 201 723 2239
Fax: +49 201 723 5409
E-mail: uwe.hillen@uk-essen.de

¹Information Network of Departments of Dermatology (IVDK), University of Göttingen, Göttingen

Accepted for publication 20 May 2009
Allergy 2010
© 2010 John Wiley & Sons A/S
DOI: 10.1111/j.1398-9995.2010.02331.x

References

1. De Cuyper C, Goeteyn M. Systemic contact dermatitis from subcutaneous hydromorphone. *Contact Derm* 1992;**27**:220–223.
2. Orjales RN, Carballada F, Carballas C, Boquete M. Codeine-induced generalized dermatitis and tolerance to other opioids. *Allergy* 2009;**64**:1692.
3. Rodríguez A, Barranco R, Latasa M, Ortiz de Urbina JJ, Estrada JL. Generalized dermatitis due to codeine. Cross-sensitization among opium alkaloids. *Contact Derm* 2005;**53**:240.
4. Hogen Esch AJ, van der Heide S, van den Brink W, van Ree JM, Bruynzeel DP, Coenraads PJ. Contact allergy and respiratory/mucosal complaints from heroin (diacetylmorphine). *Contact Derm* 2006;**54**:42–49.
5. Vander Hulst K, Parera Amer E, Jacobs C, Dewulf V, Baeck M, Pujol Vallverdú RM et al. Allergic contact dermatitis from transdermal buprenorphine. *Contact Derm* 2008;**59**:366–369.
6. Uter W, Schnuch A, Geier J, Frosch PJ. Epidemiology of contact dermatitis. The Information Network of Departments of Dermatology (IVDK) in Germany. *Eur J Dermatol* 1998;**8**:36–40.