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Allergic contact dermatitis caused by transdermal buprenorphine

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Buprenorphine is a potent semisynthetic opioid analgesic that is widely used to treat moderate to severe pain. Since 2001, it has been available in several European countries in a transdermal delivery system (TDS), and it was approved for use in the United States in 2010. We report 3 cases of allergic contact dermatitis caused by a TDS containing buprenorphine, as verified by a positive patch test reaction.

Case 1

A 56-year-old male with a history of degenerative chronic back pain had been applying transdermal buprenorphine (TDB), with good pain control. Initially, he could use the TDB patches for a week, but towards the end of the week the skin under the patch turned red and started to itch. Because of progression of the symptoms, he could finally apply the TDB for only 1 day before the TDS had to be removed because of developing dermatitis.

The patient was patch tested with the parts of the TDS containing buprenorphine (Norspan®) and fentanyl (Matrifan®), as well as with the surrounding adhesive part. Furthermore, the patient was tested with 10% buprenorphine and fentanyl, respectively in aqua and pet., in Finn Chambers® on Scanpor® tape. Patches were applied to the upper back and occluded for 48 hr, and readings were performed on D2 and D4/5 according to the recommendations of the International Contact Dermatitis Research Group. No other patch test series were tested. The test was strongly positive

for the buprenorphine 10 µg/hr TDS and buprenorphine in aqua (10%), but negative for all other tested substances.

Case 2

A 38-year-old female suffered from chronic pain in her right lower limb following surgical treatment of a herniated disc. Treatment included a permanent epidural stimulator and pain medication, including both oral buprenorphine and TDB. However, the patient developed an itch on the site of the stimulator, which was then removed. She reported severe skin irritation on the site of the TDB.

The patient was tested with both the part of the TDS containing buprenorphine and with the surrounding adhesive part. Patch testing was performed with the baseline, antimicrobial, plastic and glue, rubber and metal series, and parts of the neurostimulator. The tests were performed as described for patient 1. On D5, the test was strongly positive for the buprenorphine 5 µg/hr (Norspan®) TDS but not for the adhesive only. All other tested substances gave negative results. The patient was using oral buprenorphine 0.4 mg up to four to six times daily (Temgesic®) without signs of systemic contact dermatitis, either before or after patch testing.

Case 3

A 47-year-old male with a previous history of polymorphic light eruption and ultraviolet B hypersensitivity developed complex regional pain syndrome in his left thigh following an operation for a split peroneus brevis tendon in 2009. Initially, he was given TDB 10 µg/hr without tolerability problems, but with insufficient pain control. Three weeks later, the TDB was switched to 20 µg/hr. In the second week of treatment with the higher dose, the skin under the TDB was irritated when the TDB was removed, and, at the same time, the area where the previous TDB had been

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fastened turned red. The third TDB caused dermatitis after 2 days, and was removed.

The patient was tested with both the parts of the TDS containing buprenorphine 10 and 20 µg/hr (Norspan®) and with the surrounding adhesive part. The patient was also tested with 10% buprenorphine in aqua and pet., as described for patient 1 (Fig. 1). To test for cross-reactivity, patch tests with morphine hydrochloride 2 mg/ml, tramadol hydrochloride 50 mg/ml, oxycodone hydrochloride 10 mg/ml and codeine phosphate hemihydrate 1% and 3% in pet. were performed. We also tested fentanyl 50 µg/ml with a prick test, with an intracutaneous test (for both immediate allergy with a 30-min follow-up and delayed allergy with a 2-day follow-up), and as a patch test with transdermal adhesive (Durogesic®, 12 µg/hr). Patch testing was performed with the baseline, antimicrobial, topical medicament and plastic and glue series. On D5, the test was strongly positive for the buprenorphine 10 and 20 µg/hr TDS, but negative for the adhesive only. Buprenorphine also gave a positive result in aqua and pet. solutions. All other tested substances gave negative results.

Discussion

A delayed type IV allergic reaction to buprenorphine was verified by a positive patch test reaction in all three cases. Only 8 cases of patch test-proven allergic contact dermatitis caused by buprenorphine have previously been described in the literature (1–5). Our patients were all collected in a time frame of 3 years (2010–2012) from a single hospital district, raising the question of whether contact allergy to buprenorphine might be more common than previously suspected.

Our second patient was given both TDB and oral buprenorphine, but only developed skin symptoms with TDB. Patients who are contact-sensitized to a topically administered drug often develop systemic contact dermatitis when the same drug is administered orally (6). Recently, Kaae et al. reported on 54-year-old woman with contact dermatitis caused by TDB (Norspan®, 10 µg/hr), verified by a positive patch test

reaction (+) to buprenorphine 0.3 mg/ml in pet. (4). The patient was then prescribed oral treatment with tramadol retard (200 mg twice daily). Within 24 hr of treatment, a systemic allergic dermatitis reaction was observed at the site of the Norspan® TDS. In contrast, one of our patients tolerated a moderately high oral dose of buprenorphine without skin symptoms, indicating that systemic contact dermatitis caused by buprenorphine does not always develop in skin contact-sensitized patients.

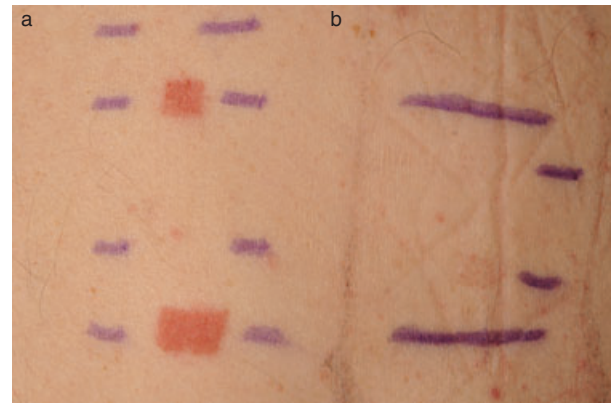


Fig. 1. (a) Positive patch test reactions to buprenorphine 10 and 20 µg/hr. (b) Negative result with fentanyl 12 µg/hr.

For clinicians, it is important to know what medication can be used as a replacement in cases of contact allergy. Two of our patients were also tested for contact allergy to fentanyl, but both patients tolerated transdermal fentanyl despite having contact dermatitis caused by TDB. Patch test cross-reactivity between codeine, morphine and heroin has been reported (7, 8), whereas no cross-reactivity has been reported between chemically unrelated opioids, such as fentanyl or tramadol (7, 8). Our cases confirm these previous reports that patients developing contact dermatitis with TDB probably tolerate transdermal fentanyl. Our third patient did not react to morphine, oxycodone, tramadol, or codeine.

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