

Allergic Contact Dermatitis from Buprenorphine and Oral Tolerance to Other Opioid Derivatives in Three Patients

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Key Words

Contact allergy · Oral opioids · Buprenorphine

Abstract

Transdermal buprenorphine (TDB) is a widely used analgesic for moderate pain. TDB is generally well tolerated, but both irritant and allergic contact dermatitis occur at patch application sites. Oral opioid tolerance in patients with allergic contact dermatitis to TDB remains controversial. Here, we describe 3 patients with allergic contact dermatitis to TDB who subsequently used oral opioid derivatives without adverse reactions. Thus, oral intolerance to opioid derivatives is not a rule in patients with allergic contact dermatitis to TDB, but the possibility should be taken into consideration.

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Introduction

Transdermal drug delivery systems are widely used for controlling moderate to severe pain. First-pass metabolism and fluctuating concentrations can be avoided when using transdermal dosage. However, irritant and allergic contact dermatitis occurs at application sites in patients using transdermal therapeutic systems [1]. Buprenorphine is highly lipophilic and thus an

ideal molecule for transdermal delivery [1, 2]. In general, transdermal buprenorphine (TDB) is well tolerated. However, irritant contact dermatitis may occur when using TDB. Allergic contact dermatitis, which is diagnosed with patch testing, is relatively rare [1]. Oral opioid tolerance in patients with allergic contact dermatitis to TDB remains controversial [3, 4]. After informed consent, we describe 3 patients with allergic contact dermatitis to buprenorphine who have subsequently used oral opioid derivatives without adverse reactions.

Case 1

A 45-year-old female without any history of adverse drug reactions was referred to us because of intolerance to TDB patches (10 µg/h Norspan[®], Mundipharma Finland). She had suffered from fibromyalgia syndrome and mental health problems. She had had a chronic wound and neuralgia on her ankle for 5 years resulting from a violent assault. Her pain had previously been treated with a maximum dose of paracetamol-codeine, but 4 months ago TDB had been introduced instead. After a month, pruritic and vesicular erythema developed at the TDB contact sites within 2–3 days; in primary health care this was considered an irritant reaction, and TDB was continued. However, the patient

thereupon removed the patches after a few days, and sufficient pain control was not achieved. In accordance with the recommendations of the International Contact Dermatitis Research Group [5], the patient was tested with baseline and cosmetic series, 5 µg/h TDB and a placebo transdermal delivery system (PTDS) provided by the manufacturer. A positive reaction (++) was observed only to TDB. Testing with the PTDS was negative. Due to her history of substance abuse, only paracetamol-codeine was prescribed with no adverse effects, and she was referred to physical rehabilitation to manage her pain.

Case 2

A 54-year-old male with intervertebral disk disorder had used TDB (Norspan) patches for 3 months. After swimming in a public pool, a patch became detached and a bullous erythema developed in the area of the patch. Similar skin eruptions also arose at the sites where the TDB patches had formerly been located. The use of TDB was withdrawn. The patient was tested negative for baseline and plastics and glues series. Testing with a PTDS remained negative, and since he had had bullous reactions to TDB, it was decided not to test him for TDB. However, he attempted to use TDB once again on his own; within days, he de-



Fig. 1. a Contact dermatitis at the site of a TDB patch. **b** Reactivation of contact dermatitis at previous buprenorphine patch sites.

veloped erythema at the site of the new patch (fig. 1a) and at all the other sites previously used for TDB patches (fig. 1b). A combination of tramadol and etoricoxib was prescribed, and no adverse reactions have appeared.

Case 3

A 47-year-old female with suspected contact dermatitis to nickel sulfate had used TDB (Norspan) patches for musculoskeletal pain for several months. At first, she had itching at the site of a patch, but later on a vesicobullous reaction developed. The patient was tested for baseline, cosmetics, and plastics and glues series with a positive reaction to nickel sulfate, as expected. Testing with a PTDS was negative, but when tested with TDB a positive reaction (++) was observed. She has now used both tramadol and oxycodone with no adverse reactions.

Discussion

A few cases of contact dermatitis from buprenorphine have been described [3, 4, 6, 7]. TDB has been described to cause allergic contact dermatitis mostly at the application site, but 2 cases of generalized eczema have been reported [4].

Buprenorphine belongs to the group of phenanthrenes, prototypical opioids that include codeine, morphine and oxycodone. Tramadol is a 4-phenyl-piperidine analogue of codeine, but does not fit into any standard classes of opioids [8]. In most cases patients were switched to either transdermal fentanyl or tramadol hydrochloride with no further adverse drug reactions. However, one patient with strong patch test positivity to buprenorphine developed systemic contact dermatitis after oral tramadol exposure, but did not react to morphine, for example [3]. Like in most cases described in the literature, the tramadol they were switched to was well tolerated by our patients 2 and 3; in addition, our patient 3 has since used oxycodone with no adverse effects.

Previously, cross-reaction in patch tests has been reported between codeine, morphine and diacetylmorphine [9, 10]. After contact allergy to buprenorphine had been confirmed, our patient 1 was treated with codeine only with no flare-ups of allergic contact dermatitis. Thus, a cross-reaction between systemic codeine and TDB could not be observed in this patient, even though the opioids are structurally similar. Contact allergy to TDB might be an underestimated problem as these allergic reactions can be interpreted as irritant reactions in primary health care. Oral intolerance to other opioid derivatives is not a rule in pa-

tients with allergic contact dermatitis from buprenorphine, but caution or an oral challenge should be considered prior to further opioid use.

Disclosure Statement

Conflict of interest: none.

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