

Allergic Contact Dermatitis from EMLA Cream in a Hemodialyzed Patient

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The eutectic mixture EMLA cream has many medical uses, including pain relief for hemodialyzed patients prior to cannulation. Cutaneous side effects associated with its application have rarely been reported. A patient on hemodialysis developed an itchy eruption over his brachial arteriovenous fistula, where he was applying EMLA cream three times per week, prior to puncture for hemodialysis. Patch testing elicited a positive reaction to several allergens, including EMLA cream "as is" and prilocaine. The lesions resolved after topical treatment with corticosteroids.

HEMODIALYZED PATIENTS may present diverse cutaneous reactions in relation to the topical application of many substances. These include local anesthetics, widely used for providing pain relief to patients undergoing hemodialysis.

EMLA cream (AstraZeneca Farmaceutica, Madrid, Spain), whose name is an acronym for "eutectic mixture of local anesthetics" (ie, prilocaine and lidocaine), was first commercialized in 1984 and is available as cream and as patches. It is widely used prior to several medical procedures, such as venipuncture, lumbar puncture, laser therapy, curettage of molluscum contagiosum, vaccination, skin biopsy, intra-dermal testing, cryosurgery, and therapy with botulinum toxin¹ (Table 1).

We report a case of contact dermatitis induced by EMLA cream in a hemodialyzed patient with a positive patch-test reaction to prilocaine and polysensitization to other allergens without present relevance. We did not find positive reactions to other local anesthetics.

Case Report

A 67-year-old patient with a personal history of systemic scleroderma and chronic renal failure and who had been

in hemodialysis since 2004 presented with an itchy, erythematous, and desquamative lesion on the anterior aspect of the left forearm, where the patient had applied EMLA cream 1 hour before every cannulation for hemodialysis, three times per week during the previous 5 months.

The lesions resolved after the withdrawal of EMLA cream and after topical treatment with prednicarbate.

The clinical diagnosis was allergic contact dermatitis from EMLA cream. Patch testing was performed with the standard series of the Grupo Español de Investigación de Dermatitis de Contacto (GEIDC), corticosteroids, local anesthetics, emulsifiers and vehicles, antimicrobials, and EMLA cream "as is." Evaluation was at 48 and 96 hours, in accordance with international recommendations. The results are summarized in Table 2.

Results of initial patch testing with the local anesthetics series (Trolab [Hermal, Reinbek, Germany] and Martí Tor [Martí Tor-I, Barcelona, Spain]), including tetracaine 1%, benzocaine 5%, cinchocaine 5%, lidocaine 5%, procaine chloride 1%, and polidocanol, were negative at 96 hours.

Patch tests with EMLA cream "as is" elicited an allergic reaction at 96 hours. The patient was subsequently patch-tested with prilocaine (0.5%, 1%, and 5% in petrolatum [pet]), and there was a strongly positive reaction at 96 hours.

Once the patient stopped using EMLA cream, no recurrence was observed.

Discussion

Traditionally, local anesthetics are divided into two main groups on the basis of their chemical structure: esters and

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Table 1. Current Uses of EMLA Cream*

Venipuncture
Lumbar puncture
Laser therapy
Curettage of molluscum contagiosum
Vaccination
Skin biopsy
Intradermal testing
Cryosurgery
Hemodialysis
Botulinum toxin therapy
Treatment of postherpetic neuralgia

EMLA Cream is used prior to the listed procedures.

amides (Table 3). Allergic reactions to members of the amide group are infrequently encountered.²⁻⁴ To date, Waton and colleagues have compiled only nine cases of cross-reaction between anesthetics of the amide group.⁵ Lidocaine (also known as lignocaine or Xylocaine [Astra-Zeneca]) and prilocaine are both members of this group and are the active principles of EMLA cream. Other components are polyoxyethylene fatty acid esters (Arlatone 289), carboxypolymethylene (Carbopol 934), sodium hydroxide, and distilled water. Allergic contact dermatitis from EMLA cream excipients has not yet been described.

Table 3. Classification of the Local Anesthetics Used

<i>Ester Group</i>	<i>Amide Group</i>
Aminobenzoate	Dibucaine (cinchocaine)
Benzocaine	Lidocaine(lignocaine, Xylocaine)
Benoxinate	Mepivacaine
Butamben picrate	Bupivacaine
Tetracaine (amethocaine)	Prilocaine
Benzoic acid	
Cocaine	
Hexylcaine	
Piperocaine	

The application of EMLA cream has been related to the development of mild and transient local adverse reactions, mainly erythema, pallor, pruritus, edema, pain, and burning. It can rarely produce methemoglobinemia in young infants.⁶ Purpura^{6,7} and contact urticaria⁵ have also been described.

Allergic contact dermatitis induced by EMLA cream is an infrequent finding, accounting for less than 0.1% of the total adverse reactions related to the use of this product.⁸ In the medical databases (*PubMed* listings from 1989 to 2005), we could only find four references to allergic contact dermatitis associated with the application of EMLA cream. Ismail and Goldsmith described the case of a child with

Table 2. Patch-Test Results

<i>Series</i>	<i>Allergens</i>	<i>Readings</i>		
		<i>48 h</i>	<i>72 h</i>	<i>96 h</i>
Spanish standard series	Carba mix	+	—	+
	Tixocortol pivalate 0.1%	++	—	++
	Mercury	+	—	+
	Wool alcohol 30%	++	—	++
Vehicles, emulsifiers (Chemotechnique)	Lanolin 100%	++	—	++
	Amerchol L-101 1%	++	—	++
	Wool alcohol 30%	++	—	++
Local anesthetics	Tetracaine 1%, benzocaine 5%, cinchocaine 5%, lidocaine 5%, procaine 1%, polidocanol	—	—	—
Corticosteroids (Chemotechnique)	Tixocortol pivalate	++	—	++
Antimicrobial series (Trolab)	Benzalkonium chloride	++	—	++
	tert-Butylhydroquinone	++	—	++
Other	EMLA Cream "as is"	++	—	++
	Prilocaine 0.5% pet	—	++	++
	Prilocaine 1% pet	—	++	++
	Prilocaine 5% pet	—	++	++

pet = petrolatum.

β -thalassemia who had been applying EMLA cream on the injection sites of subcutaneous infusion of deferoxamine for more than a year before the onset of dermatitis.⁸ Le Coz and colleagues reported the case of a hemodialyzed patient who developed a cutaneous reaction on the sites where he had been applying EMLA before each session of dialysis.⁹

Thakur and Murali reported a case of allergic contact dermatitis in a patient receiving EMLA cream for treatment of postherpetic neuralgia.¹⁰ Van den Hove and colleagues described the case of a patient who had a painful leg ulcer and who developed allergic contact dermatitis after applying EMLA cream.¹¹

All patients had positive reactions to prilocaine and negative reactions to lidocaine and therefore had no cross-reactions between the two local anesthetics or concomitant reactions to the two.

To our knowledge, the case we describe is the second case of contact dermatitis from EMLA cream in a hemodialyzed patient who had a positive reaction to prilocaine. According to previously reported cases, patch-test results were negative with lidocaine and other caines, and cross-reactions among the tested anesthetics were not observed.

Cross-reactions with amide anesthetics are uncommon; consequently, cross-reaction groupings among amide anesthetics are not yet well established. Prilocaine was implicated in cross-reactions with lidocaine, articaine, mepivacaine, dibucaine, and bupivacaine.⁵

Given the marked structural similarity between lidocaine and prilocaine, further studies are needed to explain the reason allergic contact dermatitis from EMLA cream is related only to prilocaine as yet. Moreover, whether cross-reactivity between prilocaine and other amide anesthetics could be enhanced by parenteral rather than by topical use should also be determined.

Our patient presented sensitization to several other allergens with past or unknown relevance in relation to the cutaneous lesions for which he came to us. His positive

reactions to tixocortol and antimicrobials raise the possibility that there was a concomitant allergy to self-applied hydrocortisone (eg, tixocortol) or cleansers (antimicrobials) used to prepare the sites.

Hemodialyzed patients and those with spina bifida, vascular ulcers, or chronic eczema are at risk for sensitization to the diverse topical treatments they apply.

As patch testing is not possible sometimes, contact dermatitis induced by EMLA cream is probably misdiagnosed. Because EMLA cream is being used more often, more cases of allergic sensitization to it will likely be seen in the coming years.

References

1. Dong H, Kerl H, Cerroni L. EMLA cream-induced irritant contact dermatitis. *J Cutan Pathol* 2002;29:190–2.
2. Handfield-Jones SE, Cronin E. Contact sensitivity to lignocaine. *Clin Exp Dermatol* 1993;18:342–3.
3. Suhonen R, Kanerva L. Contact allergy and cross-reactions caused by prilocaine. *Am J Contact Dermat* 1997;8:231–5.
4. Curley RK, Macfarlane AW, King CM. Contact sensitivity to the amide anesthetics lidocaine, prilocaine and mepivacaine. *Arch Dermatol* 1986;122:924–6.
5. Waton J, Boulanger A, Trechot PH, et al. Contact urticaria from EMLA cream. *Contact Dermatitis* 2004;51:284–7.
6. Calobrisi SD, Drolet BA, Esterly NB. Petechial eruption after the application of EMLA cream. *Pediatrics* 1998;101:471–3.
7. De Waard FB, Oranje AP. Purpura caused by EMLA is of toxic origin. *Contact Dermatitis* 1997;36:11–3.
8. Ismail F, Goldsmith PC. EMLA cream-induced allergic contact dermatitis in a child with thalassaemia major. *Contact Dermatitis* 2005;52:111.
9. Le Coz CJ, Cribier BJ, Heid E. Patch testing in suspected allergic contact dermatitis due to EMLA cream in haemodialyzed patients. *Contact Dermatitis* 1996;35:316–7.
10. Thakur BK, Murali MR. EMLA cream-induced allergic contact dermatitis: a role for prilocaine as an immunogen. *J Allergy Clin Immunol* 1995;95:776–8.
11. Van den Hove J, Decroix J, Tennstedt D, Lachapelle JM. Allergic contact dermatitis from prilocaine, one of the local anesthetics in EMLA cream. *Contact Dermatitis* 1994;30:239.