



CASE REPORT

# Acute Systemic Toxicity Caused by Topical Application of EMLA Cream on a Leg Ulcer: Case Report and Review of Literature

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## ABSTRACT

**Introduction:** Systemic toxicity of eutectic mixture of local anesthetics (EMLA) cream is rare and is most commonly observed in children, for example, upon extensive application, and rarely occurs in adults with certain dispositions.

**Case Report:** We report the case of a 71-year-old man who developed methemoglobinemia and systemic intoxication upon topical application of EMLA cream for leg ulcer and stasis dermatitis prior to surgical debridement. Approximately 45 min after application, the patient was found to be in a somnolent state, was unable to articulate, and showed peripheral cyanosis. The blood concentration of methemoglobin (MetHb) was 15.1%, and therefore, a diagnosis of systemic toxicity of EMLA due to methemoglobinemia was established. After removal of the cream, oxygen was applied, and further observation revealed that the patient's

condition rapidly improved without any residue. In the following, we also discuss literature related to systemic EMLA intoxication.

**Conclusion:** EMLA cream may cause severe systemic toxicity even in adults under certain conditions, for example, when applied on damaged skin or in extensive amounts.

**Keywords:** Case report; EMLA; Systemic toxicity; Lidocaine-prilocaine

### Key Summary Points

A case of severe systemic intoxication and methemoglobinemia resulting from the topical application of an eutectic mixture of local anesthetics (EMLA) cream on a leg ulcer is described.

In this case, systemic toxicity resulted from the mistaken large-scale application of EMLA under occlusion on the damaged skin and stasis dermatitis.

EMLA cream is considered safe in adults, with cases of systemic toxicity almost exclusively linked to hair removal.

The present case illustrates that the risk factors for systemic intoxication with EMLA should be considered when applied to damaged skin.

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## INTRODUCTION

The systemic toxicity of the Eutectic Mixture of Local Anesthetics (EMLA) cream is mediated by the active ingredients of the cream, the local anesthetics lidocaine and prilocaine, which are both present at a concentration of 2.5%. Systemic toxicity of EMLA may manifest as seizures, mainly due to systemic lidocaine intoxication [1], methemoglobinemia resulting from the oxidizing properties of prilocaine, and cyanosis. Therefore, a saturation gap between pulse oximeter oxygen saturation and arterial blood gas saturation exceeding 5% may occur, as traditional pulse oximetry fails to account for methemoglobin (metHb), leading to inaccurately elevated saturation values. This also hinders any improvement in pulse oximetry despite the application of oxygen. At higher concentrations, a chocolate-like color of the blood may be observed. Risk factors for methemoglobinemia due to local anesthetic intoxication include early age, the use of high quantities of drugs over an extended area, repeated application, and mutual intake of other drugs, such as celecoxib. Moreover, skin diseases involving an impaired skin barrier increase the possibility of intoxication. Such skin conditions include eczema, psoriasis, vascular malformation, mollusca contagiosa and laser hair removal. Finally, glucose-6-phosphate dehydrogenase deficiency is also known to increase the likelihood of methemoglobinemia. Therapy for intoxication includes high-flow oxygen application, monitoring, and, in severe cases, intravenous application of methylene blue. We present a case of EMLA intoxication in a patient treated for a leg ulcer. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

## CASE REPORT

A 71-year-old male was admitted for inpatient treatment of a leg ulcer and concomitant stasis dermatitis primarily caused by arthrosis and

immobility (Fig. 1). The patient did not take any medication. However, he had a Gram-negative foot and leg infection and internal secondary diagnoses, including lung emphysema, euthyroid sick syndrome, and renal failure due to immobility in the previous year. Otherwise, the patient presented as a healthy individual and was adequately oriented to all qualities, with no circulation problems in the legs, other metabolic previous illnesses or known genetic deficiencies or family history thereof. Epicutaneous patch testing and phlebological investigation did not reveal pathological findings.

Prior to surgical debridement of the ulcer, the application of EMLA cream as local anesthesia was ordered. By mistake, EMLA cream was applied occlusively not only to the ulcer but also to the entire lower leg and foot. After 45 min, the patient was found to be in a somnolent state. He was unable to articulate, had a Glasgow Coma Scale index of 11, and showed peripheral cyanosis. The occlusive dressing with EMLA cream was immediately removed, oxygen was administered, and the patient was transferred to the university emergency unit. His MetHb blood concentration was 15.1%, and his oxygen saturation was 91%. The MetHb concentration decreased to 7% after 8 h and to 1% after 24 h. The patient's condition rapidly improved without any residue (Fig. 2).



**Fig. 1** Clinical presentation of erosive stasis dermatitis in the lower leg of the patient. Written informed consent for permission to publish was obtained from the patient

## DISCUSSION

We present the uncommon case of methemoglobinemia and systemic toxicity resulting from large-scale application of EMLA cream on the lower leg prior to wound debridement. EMLA cream is widely used for local anesthesia before small superficial surgeries. Its safety has already been studied, and several reports have demonstrated the safety of this cream, especially in the context of wound debridement [2]. However, several cases of intoxication have been reported, both for children and adults [1, 3]. In the following, selected cases will be displayed, and the safety and correct usage of EMLA cream will be discussed.

Approximately two-thirds of the reported cases of EMLA cream intoxication involved children. The most common cause of intoxication is exposure prior to circumcision [4–8]. Symptoms reported included lethargy, cyanosis, and cardiopulmonary instability. Other common causes reported in children include application prior to catheter insertion or punctation [9–12]; omission of removing EMLA cream, long duration of application [11, 12]; molluscum contagiosum removal [13–17]; underlying skin

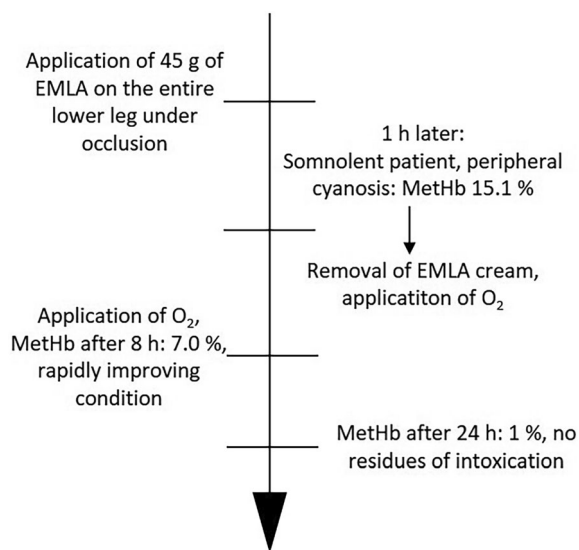
conditions with an impaired skin barrier such as eczema [13, 16]; other small interventions, such as allergy skin testing, including application over an extensive area of skin [18]; and accidental ingestion of EMLA cream, resulting in status epilepticus in a 25-month-old child [19].

In adults, the use of an EMLA cream is considered safe, and cases of systemic toxicity are almost exclusively linked to hair removal [1, 20–25]. Patients who present with systemic EMLA intoxication often have risk factors, including a damaged skin barrier due to previous treatments and the application of inappropriately high amounts of EMLA over an extended area of the skin, e.g., both legs or even the back and all four extremities [23]. However, even for patients whose face was treated for a limited amount of time (25 cm<sup>2</sup> for 30 min), there are reports of cyanosis and collapse [22]. For higher doses of local anesthetics in creams applied in the context of laser-assisted hair removal, deaths have even been reported, resulting in an Food and Drug Administration (FDA) warning for skin numbing cream in 2007 [26, 27].

The package instructions for the EMLA cream include the use of 1 g of cream for an area of 10 cm<sup>2</sup>, for a total of 10 g under occlusion. It is also advised to refrain from using EMLA cream for skin rash or eczema. Common local side effects also include purpura, skin paleness, or minor allergic reactions [28, 29].

There is a limited body of evidence concerning the absorption of active agents from the EMLA through the skin. One study investigated the absorption and suitability of EMLA for the treatment of second-degree burns [30]. Here it could be shown that prilocaine for second-degree burns has a bioavailability of up to 30%, making the possibility of intoxication unlikely. This underlines the importance of avoiding the use of EMLA cream on eczematous skin, as there might be a similar impairment of the skin barrier and therefore greater absorption.

While there are few reported cases of EMLA intoxication, it is possible that some cases were overlooked. For example, in our patient, the primary consideration was a diagnosis of excruciation under the motto “common things are common.” In such situations, the ongoing use



**Fig. 2** Timeline of events before and after systemic intoxication with eutectic mixture of local anesthetics (EMLA) cream and methemoglobinemia. *MetHb* methemoglobin

of occlusive EMLA dressings might be easily missed. Therefore, in our opinion, it is important to raise awareness of this issue.

## CONCLUSIONS

Caution should be taken when applying EMLA cream to leg ulcers. It is important to recognize that this medication functions similarly to the injection of local anesthetics and can also lead to systemic toxicity.

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**Data Availability.** Data sharing does not apply to this article, as no datasets were generated.

### Declarations

**Conflict of Interest.** Sarah Marie Hoffmann, Anna Luisa Hartmann, Pablo Nieratschker, Michael Berthold Mussler, and Christoph Mathis Schempp declare that they have no conflicts of interest to disclose.

**Ethical Approval.** Given that this was a single case report, ethics committee approval was not needed. Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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