Annals of Surgery and Perioperative Care

Open Access

Austin Publishing Group

Case Report

Unlabeled Topical Anesthetic-Induced Severe Methemoglobinemia in Pediatric Burn Patient

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Received: January 06, 2025; **Accepted:** January 28, 2025; **Published:** January 31, 2025

Abstract

The objective of this case report is to present a patient with acquired methemoglobinemia due to poisoning by unlabeled use of local anesthetics. The toxic effect of some local anesthetics leads to disruption of the processes of oxidative phosphorylation in erythrocytes with the formation of methemoglobin incapable of oxygen transport.

A 10-year-old boy suffered flamed burns with a total body surface area of 60%. While in the pediatric intensive care unit, the patient had a sudden deterioration on day 6 with cyanosis, tachycardia, hypotension, SpO_2 76% on room air; and 90% on 100% FiO_2. Telemedicine consult was requested for the acute event. During evaluations of the hypoxemia, the methemoglobin level was elevated to 22%. The source seemed to be an inadequately labeled ointment containing prilocaine used on burns as a local wound treatment.

This case underscores the importance of vigilant monitoring when using local anesthetics on burn surfaces in pediatric patients. Furthermore, global telemedicine facilitated the timely diagnosis and management of this rare but potentially life-threatening condition, methemoglobinemia.

Keywords: Methemoglobinemia; Medication labeling; Telemedicine; Topical anesthetic; Burn injury

Case Presentation

A 10-year-old boy suffered flame burns with a total body surface area of up to 60% and was treated in the Regional children's hospital ICU in Ukraine. The child's condition acutely deteriorated with central cyanosis, severe tachycardia, arterial hypotension, and a decrease in SpO_2 to 76% despite maximum therapy including intubation and ventilation with 100% FiO_2. A consult was made to a US physician via telemedicine given the relative lack of expertise in pediatric burn patients in the region. During systematic exam and laboratory evaluations of the child's hypoxemia, we discovered the methemoglobin level was elevated to 22%. Diagnosis of methemoglobinemia was made and treatment administered. To establish the cause of methemoglobinemia, we conducted a complete analysis of medications the patient had received. The source of intoxication was discovered to be an unlabeled ointment containing prilocaine that is used routinely on burned surfaces as a local wound treatment. A complete recovery was made following cessation of the application of the ointment and appropriate therapy with methylene blue 2 mg/kg over the span of 30 minutes. The patient gradually improved and stabilized within two hours. After a 45-day hospital stay, the patient was discharged home.

Discussion

In the previously mentioned case, the child almost had a potentially fatal reaction due to the administration of an unlabeled topical medication that contained local anesthetic leading to Methemoglobinemia. Importantly, this was an adverse reaction that could have been prevented had there been guidelines and monitoring to ensure the correct labeling of medications.

In general, the treatment of methemoglobinemia focuses on first discontinuing the offending drug or medication. Additionally, supportive care should be initiated with intravenous hydration, hemodynamic support with vasopressors, supplemental oxygen, and possibly mechanical ventilation as needed. First line pharmacologic intervention typically includes the use of methylene blue. This should be used when patients are symptomatic and methemoglobin levels are greater than 30%, especially when there are preexisting cardiovascular or respiratory comorbidities. Methylene blue acts by accepting an electron from NADPH, and, in its new form, leukomethylene blue reduces the 3+ ferric state back to the 2+ ferrous state in erythrocytes. Unfortunately, there are circumstances where this drug is contraindicated such as in patients with G6PD deficiency. In these cases, vitamin C can be used although it does have a slower onset of action when compared with methylene blue. The mechanism of action for vitamin C in these circumstances is by directly reducing methemoglobin because it is a natural antioxidant [1]. Other rescue therapies include hyperbaric oxygen, exchange transfusions, and in rare refractory cases VV ECMO has been utilized [2].

While this patient was fortunate to have a favorable outcome due to the wide variety of treatment options previously mentioned and the

Citation: Mahir C; Bean C and Fuzaylov G. Unlabeled Topical Anesthetic-Induced Severe Methemoglobinemia in Pediatric Burn Patient. Ann Surg Perioper Care. 2025; 10(1): 1068.

quick recognition and treatment of the condition, this is not always the case. It is important to focus on the preventative aspect of this case, especially for care provided in lower-middle income countries where treatment options may not be as readily available. Furthermore, for the exact same product or medication, there can be completely different safety guidelines on medication labeling depending on the country and its associated resources.

In many developing countries, the regulation of medicine naming, labeling, and packaging does not provide sufficient safeguards for patients. There is little recognition on the importance of human error in the selection and design of drug names, labels and packages for minimizing error potential and enhancing medication safety. Furthermore, while the evidence-base regarding the quality of professional services from pharmacies in low- and middle-income countries is limited, the existing evidence shows that standards are often deficient. In a particular study, it elucidated the lack of presence of pharmacists or other trained personnel. Also, in these low-income countries, medications are often given in incorrect dosages or the medication itself may be incorrect, and there are not typically clear guidelines for patients to follow [3]. Another important point regarding medication mislabeling is that patients will often receive medication without having any knowledge of what they received. This was the case with our patient. It is crucial that patients are aware of this information so that they feel empowered to ask questions and make informed decisions regarding their healthcare.

Medication labeling is important to consider. There is certain essential information that should be included on all medications for their safe use, and this should be presented clearly and prominently on the outer packaging. This includes items such as the generic and brand names, dosing and strength, route of administration, and specific warnings. In addition, across medications this should be standardized so that items are in a predictable location that is easy and accessible to find. There are graphic designs online which detail the correct locations for this essential information. It is important to mention, however, that certain countries may have their own unique formats or requirements that must be adhered to prior to finalizing the labeling. Nevertheless, there should be an emphasis on making this as consistent as possible within countries and between countries [4].

Highlighting these potential confusion areas and how to improve them and reduce error is important. The statistics about medication-related harm are alarming. The World Health Organization (WHO) notes that unsafe medication practices and medication errors are the leading cause of avoidable harm around the world, with costs reaching US$42 billion annually [5]. Countries are starting to work towards the goal of improving medication safety. For example, an institute in Canada named the Canadian Patient Safety Institute is leading the Canadian arm of the WHO's "Medication without Harm" campaign. They are utilizing strategies such medication review, the "5 Questions to Ask About Your Medications" program, and opioid stewardship initiatives to improve opioid safety and appropriate treatment of pain [6]. In Australia, the Pharmaceutical Society of Australia (PSA) and the Society of Hospital Pharmacists of Australia have been lobbying the government to take note of medication-related issues and in response the government has recently announced that it would make medication safety a national health priority [7].

While this is a step in the right direction, it is certainly not widespread amongst developing countries yet. More funding and research need to be devoted to safe medication labeling naming, and packaging to prevent poor patient outcomes as seen with our case. These errors risk patient safety and put a huge burden on healthcare systems globally with increased admission rates and healthcare spending. It is especially important that countries which are under resourced also find ways to be able to adhere to these practices as they are just as likely, if not more, to have these medication errors.

This case also highlighted the importance and utility of global telemedicine in the clinical setting.

Telemedicine can provide access to care in populations such as this one where there may not be healthcare providers or subject matter experts readily available. While this is especially useful for low- middle income countries, this can be helpful even when thinking about higher income countries in more rural or impoverished areas. Many research articles, especially during the COVID-19 pandemic, have investigated telehealth. In one literature review, patients had a 90% satisfaction with telemedicine and some of the benefits included the ability to make a correct diagnosis to resolve the condition, efficient mobilization of healthcare resources, increased accessibility for patients, and increased service utilization. However, there were still some challenges and barriers such as inaccessibility, low technological literacy and lack of support, poor security standards and technological concerns, loss of interest by the patients, and income impacts on physicians [8].

In conclusion, this case underscores the importance of monitoring local anesthetics used on pediatric burn surfaces and recognizing methemoglobinemia as a potentially fatal complication. Furthermore, it highlights the role of telemedicine in improving care in underserved areas and advocating for improved and equitable global medication safety.

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