Methemoglobinemia after Local Anesthesia with Prilocaine: A Case Report

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ABSTRACT
Introduction: Methemoglobinemia due to local anesthesia is a rare phenomenon. Grey–blue cyanosis that is unresponsive to oxygen therapy after the administration of local prilocaine should be considered with methemoglobinemia due to local anesthesia, and methylene blue should be considered for treatment.

Case Report: A 19-year-old man was admitted to Bakırköy Dr. Sadi Konuk Training and Research Hospital emergency department with complaints of shortness of breath, bruising of the lips and nail, palpitations, and numbness in the extremities. Toenail shooting with local anesthesia was performed 3 h prior. On admission, he was restless. Cyanosis persisted on the limb and nails, and oxygen saturation was 78% by pulse oximetry under oxygen supplementation. We found the following results on physical examination: blood pressure, 115/77 mmHg; pulse, 123/min; and respiratory rate, 28/min. Arterial blood gas analysis revealed the following: methemoglobin level, 12.4%. Following the diagnosis of prilocaine-induced methemoglobinemia, he was treated using intravenous methylene blue, and his symptoms resolved.

Conclusion: Methemoglobinemia, a rare clinical complication of local anesthesia, can be prevented by limiting the applied dose of local anesthesia. Treatment with methylene blue should be kept in mind along with supplemental oxygen therapy for patients with methemoglobinemia.

Keywords: Methemoglobinemia, methylene blue, local anesthesia
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Introduction
For erythrocytes, which contain hemoglobin, to carry oxygen to tissues, the iron content of hemoglobin should be in the form of a ferrous ion (Fe+2). Fe+2 of hemoglobin is oxidized to ferric iron (Fe+3) as a result of various oxidative stresses and methemoglobin is formed (1). Methemoglobin releases oxygen (O2) less efficiently to tissues and causes tissue hypoxia (2). Methemoglobinemia may occur because of hereditary or acquired reasons. The acquired form is more common than the congenital form. Many chemical substances or drugs that cause methemoglobinemia have been reported, such as nitrites, sulfonamides, chloroquine, aminobenzenes, and some local anesthetics (2, 3). Prilocaine is an anesthetic agent widely and safely used as a local anesthetic. It is a rare cause of methemoglobinemia, which is an uncommon cause of cyanosis (3-5). In this report, the case of a healthy adult who developed methemoglobinemia after the administration of local prilocaine before toenail shootings and who was successfully treated with methylene blue and general supportive therapy is reported.

Case Report
A 19-year-old man was admitted to Bakırköy Dr. Sadi Konuk Training and Research Hospital emergency department with complaints of shortness of breath, bruising of the lips and nail, palpitations, and numbness in the extremities. It was learned that 3 h prior, he had received 120 mg (60 mg for both nails) prilocaine (Cytanest 2%; Astra Zeneca, İstanbul, Turkey) for local anesthesia before toenail shooting.

We found the following results on physical examination on admission; he was restless, conscious, oriented, and cooperative; he showed the following vital signs: blood pressure, 115/77 mmHg; pulse, 123/min, and respiratory rate, 28/min. Cyanosis persist-
Methemoglobinemia due to the local anesthetic was suggested, and the patient was admitted to the emergency observation room for follow-up and treatment. At the first hour of treatment, intravenous saline infusion and oxygen via facemask were given because the methemoglobin level was lower than 20% and the vital signs because stable.

After 1 h of treatment, the patient still had palpitation, numbness in the extremities, and peripheral cyanosis. As the next arterial blood gas analysis showed the following: pH, 7.36; pO2, 64 mmHg; sO2, 73.8%; pCO2, 41.2 mmHg; HCO3 level, 21 mmol/L; and methemoglobin-level, 12.4%.

In our case, 120 mg of prilocaine was subcutaneously administered prior to both toenail shooting, and after 3 h, he had bruising of the lips and nail, shortness of breath, headache, and numbness in the extremities. The patient, who did not have any additional disease and who previously received local anesthetics, was considered to have acquired methemoglobinemia; this diagnosis was confirmed with arterial blood gas analyses. Local cream has been reported to contain prilocaine, and it also may cause methemoglobinemia (3). In literature, it is not specified whether methemoglobinemia is related to the doses of prilocaine. However, the administration prilocaine to both lower extremities at the same time to our patient may increase the risk of methemoglobinemia (7).

Supplementary oxygen therapy is the most important step for the treatment of methemoglobinemia. Intravenous methylene blue is the first agent of choice; however, there are some studies where ascorbic acid was used for the treatment of methemoglobinemia (3, 4). Methemoglobin can slowly oxidize to hemoglobin; thus, administering intravenous methylene blue can accelerate this process. The capacity of oxygen transport is slightly reduced in healthy humans; therefore, these patients are usually asymptomatic. In some cases, oxidant removal is sufficient for treatment (9). In some studies, the first dose of methylene blue is between 0.5 to 5.5 mg/kg, while the total dosage is between 0.6 and 9.4 mg/kg (3, 5, 9).

The level of methemoglobin of our patient decreased from 12% to 10% with supplementary oxygen therapy and saline infusion in the first hour. Intravenous methylene blue (1 mg/kg) was administered for at least 10 min to the patient because the symptoms still persisted. The symptoms and complaints of the patient regressed 1 h after the administration of methylene blue, and the level of methemoglobin decreased to less than 1%.

The transformation of methemoglobin to hemoglobin starts in 15–60 min in patients administered methylene blue. Methylene blue is

Discussion

Under physiological conditions, methemoglobin amounts less than 2–3% of the total hemoglobin. Methemoglobin is a non-functional hemoglobin derivative where the hemeiron is oxidized from Fe^{2+} to Fe^{3+}. When the methemoglobin concentration in erythrocytes increases to 1–2 g/100 mL (6–12% of the total hemoglobin), cyanosis becomes apparent (1, 6). Methemoglobinemia, central nervous system toxicity, and cardio toxicity are rare side effects due to local anesthetics. Grey–blue central cyanosis, which is unresponsive to oxygen therapy, is a valuable clinical finding (6, 7). Headache, tinnitus, numbness of the lips, dizziness, lethargy, weakness, confusion, and dyspnea may be observed at higher concentrations of methemoglobin. Respiratory depression, cardiac arrhythmias, convulsion, and coma may occur below a 50% level, while concentrations above 70% may be fatal (7). Methemoglobinemia occurs in congenital deficiency of NADH-diaphorase, cytochrome b5, glucose-6-P dehydrogenase, and in the presence of abnormal hemoglobin (1, 3). The concentration of methemoglobin is usually kept under 1.5–2% by the methemoglobin reductase system in erythrocytes in healthy people who use oxidants such as drugs, foods, or chemical substances (8). In adults, methemoglobin is formed due to toxicological agents such as drugs, especially local anesthetics. Prilocaine is commonly used for local surgeries. It is an amide-type local anesthetic and is hydrolyzed in the liver. O-toluidine, a degradation product of prilocaine, has a long half-life time and has an accumulation trend. It oxidizes hemoglobin and causes methemoglobinemia (3).
contraindicated in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency; in patients known to have G6PD deficiency, ascorbic acid should be used instead of methylene blue (3, 9). Hyperbaric oxygen therapy and exchange transfusion may become necessary if the level of methemoglobin remains over 70% (10).

**Conclusion**

Using the minimum dose of local anesthetics can prevent methemoglobinemia, which is a rare complication of local anesthetics. In addition, after prilocaine application for minor surgery, patients should be observed for at least 1 h for the emergence of the clinical finding of methemoglobinemia. Methylene blue can be safely used along with supplemental oxygen therapy.

**References**