

Cost of Beauty; Prilocaine Induced Methemoglobinemia

Güzelliğin Bedeli; Prilokaine Bağlı Gelişen Methemoglobinemi Olgusu

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SUMMARY

Prilocaine induced methemoglobinemia is a rare entity. In the present paper, the authors aim to draw attention to the importance of this rare condition by reporting this case. A 30-year-old female presented to Emergency Department with headache, dispnea and cyanosis. The patient has a history of 1000-1200 mg of prilocaine subcutaneous injection for hair removal at a beauty center, 5 hours ago. Tension arterial: 130/73 mmHg, pulse: 103/minute, body temperature: 37 °C and respiratory rate: 20/minute. The patient had acral and perioral cyanosis. Methemoglobin was measured 14.1% in venous blood gas test. The patient treated with 3 gr ascorbic acid intravenously. The patient was discharged free of symptoms after 48 hours of observation. Emergency physician should consider methemoglobinemia in presentation of dispnea and cyanosis after injection of prilocaine.

Key words: Methemoglobinemia; prilocaine; cyanosis.

ÖZET

Prilokaine bağlı gelişen methemoglobinemi nadir görülen bir durumdur. Bu yazıda epilasyon öncesi kullanılan prilokaine sekonder gelişen methemoglobinemi olgusunu sunarak nadir görülen bu durumun önemine işaret etmek istiyoruz. Otuz yaşında kadın acil servise baş ağrısı, dispne ve siyanoz şikayetleri ile başvurdu. Hastaya beş saat öncesinde bir güzellik merkezinde epilasyon öncesinde yaklaşık 1000-1200 mg prilokain subkutan enjeksiyonu yapıldığı öğrenildi. Başvuruda kan basıncı 130/73 mmHg, nabız 103/dk, vücut ısısı 37 °C ve solunum sayısı 20/dk olarak kaydedilmişti. Hastanın akral siyanozu belirgindi. Venöz kan gazında methemoglobin düzeyi %14.1 olarak ölçüldü. Hastaya 3 g intravenöz askorbik asit uygulandı. Tedavi sonrası semptomları gerileyen ve komplikasyon geliştirmeyen hasta 48 saat sonra taburcu edildi. Acil servis doktorları, prilokain enjeksiyonu sonrası gelişen dispne ve siyanoz ayırıcı tanısında mutlaka methemoglobinemiye akla getirmelidirler.

Anahtar sözcükler: Methemoglobinemi; prilokain; siyanoz.

Introduction

Hemoglobin (Hb) is a molecule which carries oxygen from respiratory organs to the rest of the body. Hb binds to iron in a ferrous (Fe^{2+}) oxidation state under normal conditions. However, the existence of oxidative stress is known to transform iron to ferric iron (Fe^{3+}). Upon oxidation, hemoglobin or methemoglobin (MetHb) cannot bind to oxygen molecules. In methemoglobinemia, the Hb is unable to release oxygen effectively to body tissues. While mild forms of methemoglobinemia can be asymptomatic, cyanosis, tachypnea,

tachycardia, hypotension, confusion, and even death can be seen in the more severe cases.^[1] There are three common causes of methemoglobinemia, including hemoglobinopathies, hereditary enzyme deficiencies (NADH MetHb reductase), and exposure to drugs. Interestingly, hemoglobinopathies and hereditary enzyme deficiencies (NADH MetHb reductase) are the least common causes, whereas exposure to drugs is the most common.^[2]

Many chemicals and drugs had been reported to cause toxic methemoglobinemia, including nitrite, nitrate, chlorate, qui-

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nine, aminobenzene, nitrobenzene, nitrotoluenes, phenacetin, chloroquine, dapsone, phenytoin, sulphonamides, and local anesthetics.^[3] Methemoglobinemia, caused by prilocaine a local anesthesia is rare.^[4] Prilocaine, a derivative of toluidine, is an amide local anesthetic and has been shown to produce high MetHb levels.^[2,5] Because of its rarity, our knowledge about treatment use is limited. In this paper, we discuss a treatment strategy using ascorbic acid for a patient diagnosed with methemoglobinemia by prilocaine. Research targets and strategies to understand best treatment strategies will be discussed.

Case Report

A 30-year-old woman was admitted to emergency department (ED) with complaints of tachycardia, headache, dyspnea, and cyanosis. It was learned from her history that she was anesthetized with 2.5-3 vials (1000-1200 mg?) of prilocaine (citanest®) subcutaneously before a laser hair removal procedure. Although the severity of the symptoms decreased at the time of ED admission compared to the initial time point, her symptoms were still ongoing. The patient's medical history was unremarkable. The tension arterial rate was 130/73 mmHg, pulse rate was 103/minute, body temperature was 37 °C, and respiratory rate was 20/minute. The pulse oximeter measured O₂ saturation as 90%, and she had acral cyanosis. Electrocardiography revealed sinus tachycardia with a rate of 103/minute. Chest radiograph, complete blood counting, renal function tests and electrolytes were all in the normal range. Venous blood gas analyses revealed MetHb as 14.1%. Despite treatment with 4 L/minute O₂, her symptoms were still continual. She was admitted to the intensive care unit and 3 grams of ascorbic acid was given intravenously. Two hours after treatment, control MetHb was measured as 2.4%, and the patient was free of symptoms and with no complications. She was discharged as healthy upon a 48 hour of follow up period.

Discussion

Prilocaine at therapeutic doses (1-2 mg/kg) can cause limited methemoglobinemia without cyanosis.^[6] The maximum safe dose of prilocaine is 8 mg/kg (maximum of 600 mg) as a single injection.^[2] In this case, 1000-1200 mg of prilocaine was administered, in which the limits were highly exceeded. The effects of local anesthetic induced methemoglobinemia are known and include seizures, respiratory compromise, myocardial infarction, shock state, coma, hypoxic encephalopathy, and death. In a retrospective study it was reported that most patients with a methemoglobin ($\geq 8\%$) were symptomatic.^[7]

In methemoglobinemia resulting from chemical substances,

the first step of treatment is to avoid further exposure. If methemoglobinemia is under 20%, spontaneous recovery is usually observed after drug avoidance, but treatment may be necessary in newborns and infants.^[8] Methylene blue, ascorbic acid, and riboflavin have been suggested as treatment modalities.^[9] Methylene blue should be administered 1-2 mg/kg intravenously in five minutes, and repeated one hour later if adequate improvement is not observed.^[10] It is contraindicated in patients with glucose 6 phosphate dehydrogenase deficiency because administration of methylene blue can cause aggravation of methemoglobinemia, chest pain, cyanosis and hemolytic anemia.^[3] In such cases, ascorbic acid can be considered as an antidote.^[11,12] Hyperbaric oxygen therapy and exchange transfusion is another option if MetHb level is over 70%.

Ascorbic acid reduces MetHb by a non-enzymatic processes in animal and human erythrocytes in vitro, which makes ascorbic acid a candidate for treatment of methemoglobinemia.^[13,14] It is most commonly used orally in long term treatment of patients with hereditary methemoglobinemia.^[1] Although, methylene blue can be a first choice treatment of methemoglobinemia, if there is limited experience in the use of ascorbic acid in toxic methemoglobinemia.^[15] Although MetHb was measured relatively less (14.1%) in the present case, there was an indication of antidote therapy due to the patient being symptomatic. In addition, ascorbic acid was chosen because a limited supply of methylene blue in the hospital. After administration of ascorbic acid, MetHb was measured as 2.4% and she was asymptomatic. Aydogan et al. reported that two patients with methemoglobinemia recovered after ascorbic acid administration.^[13] Tekbas et al. also reported an improvement in a patient with combined treatment of methylene blue and ascorbic acid caused by methemoglobinemia due to prilocaine given before intravascular laser therapy.^[16]

Conclusion

Methemoglobinemia resulting from the usage of prilocaine within and out of hospital is a major concern. Methemoglobinemia should be considered in patients who had cyanosis after local anesthetic administration. In cases which methylene blue could not be used as an antidote, ascorbic acid can be a safe alternative.

Conflict of Interest

The authors declare that there is no potential conflicts of interest.

References

1. Honig GR. Hemoglobin disorder. In: Behrman RE, Kleigman

- RM, Jenson HB, editors. Nelson textbook of pediatrics. Philadelphia: Saunders; 2004. p. 1478-88.
2. Aygencel SG, Akinci E, Pamukcu G. Prilocaine induced methemoglobinemia. *Saudi Med J* 2006;27:111-3.
 3. Tabel Y, Sandikkaya A, Gungor S, Ozgen U. Methemoglobinemia after injection of prilocaine for pre-medication of circumcision. [Article in Turkish] *J Dicle Med School* 2009;36:53-5.
 4. Coleman MD, Coleman NA. Drug-induced methaemoglobinemia. Treatment issues. *Drug Saf* 1996;14:394-405. [CrossRef](#)
 5. Kreutz RW, Kinni ME. Life-threatening toxic methemoglobinemia induced by prilocaine. *Oral Surg Oral Med Oral Pathol* 1983;56:480-2. [CrossRef](#)
 6. Warren RE, Van de Mark TB, Weinberg S. Methemoglobinemia induced by high doses of prilocaine. *Oral Surg Oral Med Oral Pathol* 1974;37:866-71. [CrossRef](#)
 7. Guay J. Methemoglobinemia related to local anesthetics: a summary of 242 episodes. *Anesth Analg* 2009;108:837-45.
 8. Mansouri A, Lurie AA. Concise review: methemoglobinemia. *Am J Hematol* 1993;42:7-12. [CrossRef](#)
 9. Akinci E, Yüzbaşıoğlu E, Aslay S, Coşkun F. Incidence of metoclopramide-induced methemoglobinemia. *Turk J Emerg Med* 2011;11:49-53. [CrossRef](#)
 10. Ryoo S, Sohn Ch, Oh B, Kim W, Lim K. A case of severe methemoglobinemia caused by hair dye poisoning. *Hum Exp Toxicol* 2014;33:103-5. [CrossRef](#)
 11. Gülgün M, Kul M, Sarıcı S. Prilocaine-induced methemoglobinemia: report of two cases and review of literature. *Erciyes Tıp Dergisi (Erciyes Medical Journal)* 2007;29:322-5.
 12. Öztürk E, Aktaş BT, Öztarhan K, Adal E. Lokal anestezi uygulaması sonrası gelişen methemoglobinemi. *Jopp Rerg* 2010;2:46-8.
 13. Aydoğan M, Toprak DG, Turker G, Zengin E, Arısoy ES, Gokalp AS. Intravenous ascorbic acid treatment in prilocaine-induced methemoglobinemia: report of two cases. [Article in Turkish] *Cocuk Sagligi ve Hastaliklari Dergisi* 2005;48:65-8.
 14. den Boer PJ, Bleeker WK, Rigter G, Agterberg J, Stekkinger P, Kannegieter LM, et al. Intravascular reduction of methemoglobin in plasma of the rat in vivo. *Biomater Artif Cells Immobilization Biotechnol* 1992;20:647-50.
 15. Ballin A, Brown EJ, Koren G, Zipursky A. Vitamin C-induced erythrocyte damage in premature infants. *J Pediatr* 1988;113:114-20. [CrossRef](#)
 16. Tekbas G, Oğuzkurt L, Ozkan U, Gurel K. Prilocain-induced methemoglobinemia after endovenous laser ablation. *J Vasc Interv Radiol* 2010;21:758-9. [CrossRef](#)