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Acute toxic methemoglobinemia caused by a topical anesthetic

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Abstract

A case is presented in which respiratory distress resulted from the production of methemoglobin following application of topical benzocaine to a child's oral mucous membrane.

Modern local anesthetics are among the safest of administered agents, with few reported cases of morbidity or mortality. The use of topically applied local anesthetic agents is important in the atraumatic administration of regional block anesthesia and for performing minor procedures. Topical anesthetics poorly penetrate intact tissue but can penetrate abraded skin or injured mucous membranes.

Concentrations of agents used for topical application are considerably higher than those of the same agent when used for injection. The higher concentration of these agents also leads to a greater potential toxicity. Because topical anesthetics generally are vasodilators, vascular absorption can be rapid, and levels in the blood quickly may reach those achieved by direct intravenous administration.

Topical anesthetics are available in ointments, gels, or pressurized spray containers. These dosage forms can present difficulties in determining accurately the amount of anesthetic a patient receives during a procedure. This report presents just such a situation — a case in which severe systemic effects resulted from application of the topical anesthetic benzocaine.

Literature Review

Acute toxic methemoglobinemia is a potentially fatal disorder. Methemoglobin is formed when the iron in the hemoglobin complex is changed from the ferrous (Fe^{+2}) to the ferric (Fe^{+3}) state.[1,2] The Fe^{+3} hemoglobin molecule cannot bind reversibly with either oxygen or carbon dioxide, and, therefore, it becomes useless in the transport of respiratory gases.

A number of drugs and chemicals such as phenacetin, amyl nitrate, nitroglycerin, silver nitrate, and primaquine, have been implicated in precipitating acute toxic methemoglobinemia.[3] Several local anesthetics (lidocaine,[4,5] prilocaine,[6] and benzocaine[7-11]) also have been implicated in initiating acute toxic methemoglobinemia. In reported cases, lidocaine,[4,5] appears to be associated with an idiosyncratic production of methemoglobin especially in patients who have an inherited deficiency in erythrocyte metabolism, which decreases their ability to reduce methemoglobin to hemoglobin. In contrast, prilocaine[6] and benzocaine[7-11] precipitate the production of methemoglobin in normal individuals in direct relation to the absorbed dose of the drug. Potter and Hillman[9] estimate that between 15-25 mg benzocaine/kg body weight can cause significant methemoglobin formation.

Complete absorption of only 5 ml of a 20% benzocaine solution potentially can cause significant methemoglobin production in patients weighing less than 40 kg. Therefore, it is extremely important to avoid liberal use of highly concentrated topical anesthetics despite the fact that benzocaine is believed to be absorbed poorly.[12] Drug concentration, its length of time in contact with the tissues, and the degree of trauma or abrasion to the tissue surface are all factors in absorption.

The definitive test for methemoglobinemia is the methemoglobin level in venous blood assayed by spectrophotometer. Quantifying methemoglobin (particularly in the presence of other abnormal hemoglobins) requires extensive sample preparation. However, a presumptive diagnosis in an acutely cyanotic patient can be made using the "methemoglobin screen" test, in which a rapid spectrophotometric verification of the presence — not quantity — of methemoglobin can be made. Although methylene blue is recommended in the treatment for acute methemoglobinemia, in high concentrations it can induce methemoglobin formation — it must be administered with caution.

Case Report

An apprehensive 5½-year-old male presented in the oral surgery clinic for removal of maxillary and mandibular arch bars. These were placed after reconstruction of an ankylosed mandibular condyle with a costochondral graft. The child weighed 19 kg. A topical prepara-

tion (20% by weight mixture of benzocaine with flavoring agents in a polyethylene glycol base)[a] was applied to the gingival tissue and allowed to remain in the mouth for five minutes before expectoration. Removal of the arch bars was accomplished in five minutes with minimal stress to the patient. The parents were given instructions to inform us if the child showed any unexpected symptoms such as excessive bleeding, and/or nausea and vomiting.

Approximately 15 minutes after discharge and 30 minutes after administration of the topical anesthetic, the parents returned to the clinic with the patient, who complained of nausea and dizziness. The physical examination was remarkable for profound cyanosis and agitation. A CBC was within normal limits and arterial blood gases showed a pH of 7.45, a $PaCO_2$ of 31, and a PO_2 of 78. Venous blood was drawn for a methemoglobin level and a methemoglobin "screen." Following a positive "screen" report, a presumptive diagnosis of acute toxic methemoglobinemia was made. Methylene blue was given intravenously to a total dose of 20 mg (1 mg/kg of body weight), and complete resolution of the cyanosis occurred within 15 minutes. The patient was admitted overnight for observation and discharged in the morning. The report on the methemoglobin level later revealed an elevated level of 13.8% (normal value less than 1%). Follow-up appointments showed no residual effects from the cyanotic episode.

Conclusion

A diagnosis of acute toxic methemoglobinemia should be considered when patient anxiety, dyspnea, and cyanosis is coupled with recent use of local anesthetics, particularly topical benzocaine.

[a] Hurricaine gel, Beutlich, Inc., Chicago, Ill.

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Quotable Quote

"Love of truth, sought with humility, is one of the great forces capable of bringing the men of today together across the different cultures. Science is not opposed to humanism or mysticism. All genuine knowledge opens the way to the essence of life and all truth can become universal.

. . . True research, like culture, builds up human communities regardless of frontiers."

From: An address by Pope John Paul II at the Cern Laboratory, Geneva, Switzerland, June 15, 1982.