GUEST EDITORIAL

METHEMOGLOBINEMIA IN CRITICALLY ILL BURNED PATIENTS

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Methemoglobinemia is an uncommon cause of arterial hemoglobin desaturation that should be suspected whenever a patient's low oxygen saturation (typically ~85%) as measured by pulse oximetry cannot be readily attributed to other, more expected causes. Clinical methemoglobinemia necessarily involves either increased production of methemoglobin, a genetically abnormal hemoglobin that is resistant to reduction, or decreased levels of circulating erythrocytic cytochrome-b_5 reductase. Clinicians should particularly consider a diagnosis of methemoglobinemia when a patient with unexplained low oxyhemoglobin saturation has been exposed to inducing agents, especially in high doses. Drugs capable of inducing this condition include nitrates, nitrites, sulfonamides, and 2 local anesthetics: benzocaine and prilocaine.

Because of its rare occurrence, methemoglobinemia is discussed in the medical literature predominantly in case reports such as the article by Wolak et al[1] in this issue of the *American Journal of Critical Care.* Wolak et al describe the development of methemoglobinemia in a burned patient treated with mafenide (Sulfamylon), a sulfonamide. Although previously reported by Ohlgisser et al,[2] this life-threatening condition is worthy of being reported to all disciplines of medicine.

The genetic makeup of individuals susceptible to development of methemoglobinemia remains to be determined and is currently being investigated.[3,4] Until it becomes possible and practical to identify patients at risk and avoid exposing them to inducing drugs such as mafenide, it falls to clinicians to keep this diagnosis in mind and perform arterial CO-oximetry, available in all arterial blood gas laboratories, whenever the clinical setting makes sense to consider it.

Although susceptibility to methemoglobinemia currently cannot be predicted, the relationship between dose of local anesthetics and extent of methemoglobinemia has been established. Ho et al,[5] in describing 2 patients in whom methemoglobinemia developed after topical anesthetization with benzocaine before transesophageal echocardiography, estimated that the patients had received 1200 and 1400 mg of benzocaine, equivalent to 8 and 10 one-second sprays of Cetacaine (Cetylite Industries, Inc, Pennsauken, NJ). Cetacaine, a proprietary mixture commonly used for topical mucosal anesthetization, is 14% benzocaine and 2% tetracaine. Hurricaine (Beutlich LP Pharmaceuticals, Waukegan, Ill), another proprietary mixture commonly used as a topical mucosal anesthetic, is 20% benzocaine.

Multiple reports of methemoglobinemia after exposure to a cream containing a eutectic mixture of local anesthetics, a topical skin anesthetic composed of 2.5% lidocaine and 2.5% prilocaine, point to the methemoglobinemic potential of prilocaine. In these case reports and others, lidocaine has been given along with other established inducing drugs, but I have not seen convincing evidence that lidocaine alone can produce methemoglobinemia, even in susceptible individuals.

Finally, methemoglobinemia is a diagnosis of exclusion. Even when a patient has received a drug established as an inducing agent for this condition, arterial oxygen desaturation indicated by pulse oximetry or cyanosis should, first and foremost, be considered as a failure of oxygen delivery from the lungs or oxygen carriage by the blood. Immediate investigation of usual causes and institution of treatment including enhanced oxygen inhalation, followed as soon as is practical by arterial blood gas analysis, are required first as potentially life-saving maneuvers. Only after these steps have been taken—or simultaneously with them—should CO-oximetric measurement of hemoglobin saturation be performed to make a definitive diagnosis of methemoglobinemia, and, if methemoglobinemia is present, specific treatment begun.

REFERENCES

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