When Patients Become Cyanotic: Acquired Methemoglobinemia

Methemoglobin is hemoglobin that has been oxidized. Oxidized hemoglobin cannot bind or carry oxygen because it contains ferric iron rather than ferrous iron; ferric iron causes a spatial configuration of the methemoglobin molecule’s atoms and electrons that induces the molecule to bind a water molecule. Methemoglobin normally composes less than 1 percent of circulating red blood cells. The presence of large amounts of methemoglobin causes normal hemoglobin to bind oxygen more tightly instead of releasing it for cellular use.

Chemicals that can act as oxidants can induce the formation of methemoglobin after being absorbed into the bloodstream from the gastrointestinal tract, through the skin, after an inhalation exposure or after an injection. Toxicity symptoms may be immediate or may be delayed by several hours owing to varying absorption rates. There are many medications (Please see box to the right, “Medications Associated With Methemoglobinemia”) or drug metabolites that can oxidize the ferrous-containing hemoglobin into ferric-containing methemoglobin. The administration of local anesthetics to patients who also are taking other medications associated with increased methemoglobin levels may heighten their risk of developing toxic methemoglobinemia.

The occurrence of methemoglobinemia in dental practice is a rare, but potentially life threatening, event. Reports of prilocaine-induced methemoglobinemia have prompted labeling changes for the prilocaine products Citanest Plain (Astra USA) and Citanest Forte (Astra USA). The new package labeling states: “The development of methemoglobinemia is generally dose related, but may occur at any dose in susceptible individuals. While methemoglobin values of less than 20 percent do not generally produce any clinical symptoms, the appearance of cyanosis at two to four hours after administration should be evaluated in terms of the general health status of the patient.” The accompanying dosing guidelines state that the maximum recommended dose for patients weighing less than 150 pounds (70 kg) is 4 mg/lb (8 mg/kg). The maximum dose for patients weighing 150 pounds or more is 600 mg (15 milliliters) or eight cartridges. Each 1.8 mL cartridge contains 72 mg of prilocaine.

Practitioners who use topical benzocaine or prilocaine should be aware that these products may have the potential to cause life-threatening adverse reactions.

Dentists may not become aware that their patients have these anesthetic-associated adverse drug reactions because patients often leave the office before the onset of symptoms. Before performing a dental procedure that requires the use of local or topical anesthetics, practitioners should attempt to identify patients who are at an increased risk of experiencing adverse events.

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The health status questionnaire should include questions about blood abnormalities, heart or liver problems and previous adverse drug reactions. Patients medical histories should be updated at six-month intervals. If an adverse drug reaction occurs that requires practitioner intervention so that the patient receives appropriate treatment for the reaction, the FDA Medwatch Program provides a confidential reporting mechanism that can help inform other practitioners about medication reactions such as methemoglobinemia.

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-George Carlin, American comedian