Termination of Hiccups Occurring under Anesthesia

To the Editor—Hiccups occurring during anesthesia can be problematic when the intermittent diaphragm spasm disturbs the surgical field. Hiccups can also interfere with diagnostic studies such as magnetic resonance imaging scanning and therapeutic interventions such as radiation therapy. The precise etiology of hiccups is unknown, but probably results from stimulation of one or more limbs of the hiccup reflex arc.¹

Many empirical treatments have been described for terminating undesirable hiccups during anesthesia. Parenteral administration of drugs such as ketamine,² methylphenidate,³ ephedrine, droperidol, chlorpromazine, doxapram, anticholinergics, and several muscle relaxants have been tried with variable effectiveness. The greatest success has been achieved with mechanical maneuvers that irritate or stimulate the soft palate and pharynx. This presumably interrupts the hiccup reflex by inhibiting vagal afferent impulses. The techniques described are nasopharyngeal instillations of ether⁴ or five ml ice cold saline⁵ and catheter stimulation of the nasopharynx.⁶

Although highly successful, these latter techniques can be used safely only in the awake patient or in the patient whose trachea is intubated because of the risk of airway compromise or aspiration or both. I describe here a simple, rapid-acting technique for terminating unwanted hiccups in the sedated or unconscious patient whose trachea is not intubated.

A 2-year-old child with cerebellar neuroblastoma was undergoing one of many in a series of outpatient radiation treatments. The entire procedure takes less than 10 min and is not painful, but requires precise positioning and alignment of the radiation beam. It is essential that the patient not move during radiation administration. The patient was sedated with intravenous ketamine 2 mg/kg, midazolam 0.05 mg/kg, and glycopyrrolate 0.01 mg/kg. This combination produced rapid onset and short duration of sleep with spontaneous respirations and a patent airway. Normal respirations do not displace the head position. However, when this patient began to hiccup, the diaphragmatic spasm altered the precise position of his head. Rather than intubate the trachea for such a short procedure, I passed a broken ampule of ammonium chloride ("smelling salts") under the patient’s nose. Within one respiratory cycle the hiccups abruptly ceased, and the radiation therapy proceeded without further interruption. I have since used this technique on several other patients, both awake and sedated, with 100% success and no adverse effects.

Since smelling salts usually are readily available in most hospital settings, they offer a rapid and convenient alternative method for terminating unwanted hiccups in the intubated patient.

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moglobin increased over the following 15 min from 0.98 ± 0.89 to 7.69 ± 3.73% (n = 6). When Hurricane® was sprayed through an endotracheal tube for 1 s toward the lung, methemoglobin increased to 2.6 ± 1.9% (n = 5). When the spray was directed cephalad through the tracheostomy after insertion of an endotracheal tube (with none entering the lower airway), methemoglobin increased to 9.6 ± 3.7% (n = 4). Three milliliters of 4% lidocaine sprayed into the stoma had no effect on methemoglobin (methemoglobin 0.75 ± 0.22% and control 0.65 ± 0.18% after spray, n = 5).

Topical sprays and ointments containing 14–20% benzocaine re- producibly cause dose-dependent methemoglobinemia. Fifty reports describing methemoglobinemia in association with benzocaine suggest that this is due neither to enzyme deficiencies nor to allergy, but rather is due to a direct toxic action of this drug. Benzocaine absorbed from mucous or pulmonary membranes oxidizes blood hemoglobin in proportion to the absorbed dose. Barker et al.1 used benzocaine intratra- cheally to increase methemoglobin to 70% experimentally in dogs. Potter and Hillman2 reviewed cases in which dose could be estimated and concluded that 15–25 mg·kg⁻¹ can produce recognizable cyanosis. Studies in rats suggested that each 2 mg·kg⁻¹ of benzocaine produced 1% methemoglobin. Benzocaine is more easily oxidized to methemoglobin; 2) newborns have lower levels of NADH-methemoglobin reductase, catalase, and glutathione peroxidase; and 3) dosage usually is greater per kilogram body weight. In one premature infant, benzocaine ointment increased methemoglobin to 83% when used to lubricate an esophageal stethoscope. The infant survived because of prompt use of methylene blue and 100% oxygen. The physiologic impact is greater but the detection less facile in the presence of anemia, in which a larger fraction of total hemoglobin may be oxidized.

Hurricane® is 20% benzocaine dissolved in propylene glycol with some alcohol and cherry flavoring and a propellant of dissolved propane and butane. Preparations with over 8% benzocaine include Hurricane® spray (20%), Hurricane® Topical Anesthetic Gel (20%) and Liquid (20%), Campho-phenique® Sting Relief Formula (20%), Dermoplast® Anesthetic Pain Relief Spray (20%), and Cetacaine® spray (14%). The local anesthetic, prilocaine (Cetanest®), has been reported to cause methemoglobinemia although its structure is quite different from that of benzocaine.6

In response to an advance copy to the Food and Drug Administration (FDA) of this letter, the authors learned that the FDA had convened a panel on this subject in 1979. Its conclusions, published in the Federal Register, noted that methemoglobinemia can result from its use, but did not recommend that notification of this problem be included on products.

Although death can be a complication of methemoglobinemia, no case reports of death were found in our literature search. The FDA has received 14 case reports of benzocaine-induced methemoglobinemia via the “spontaneous reporting system,” 10 of which were not among those found in our literature search. One death was reported to the FDA in 1989; however, circumstances surrounding that case are not sufficiently clear to establish a true cause-effect relationship between benzocaine and outcome.

The following are recommended:

1. Federal regulatory consideration: The Federal FDA should reconsider whether further action related to benzocaine is indicated, both for labeling and for standards limiting concentrations and over-the-counter availability.

2. Product suppliers: All products containing benzocaine in concentrations over 8% should carry suitable warning of the probability that methemoglobinemia will occur in proportion to dosage. Labels should provide information of the possible need for methylene blue treatment and the recommended dosage.

3. Information sources: The Physicians’ Desk Reference and other references should add a warning regarding methemoglobin for each product containing over 8% benzocaine and should note that methylene blue should be available for prompt administration with recommended dosage.

4. Physicians and other users: Benzocaine sprays, gels, and ointments should be avoided in infants and in patients with anemia or other diseases in which reduced oxygen transport may be of special concern. Use of benzocaine should be avoided on skin or mucosal surfaces where normal tissue barriers to absorption are impaired. In general, benzocaine should be used sparingly and cautiously and with monitoring for cyanosis. Pulse oximetry detects methemoglobinemia, albeit under-estimating its magnitude by about half in low concentrations and only indicating a saturation decrease to 80–85% with 70% methemoglobinemia. It would be prudent to administer oxygen to patients at risk of hypoxia after using benzocaine topical anesthesia.

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