A Review of Current Literature of Interest to the Office-Based Anesthesiologist

Succinylcholine Use and Dantrolene Availability for Malignant Hyperthermia Treatment. Larach MG, Klumpner TT, Brandon BW, Vaughn MT, et al. on behalf of the Multicenter Perioperative Outcomes Group. *Anesthesiol.* 2019;130:41–54.

Dantrolene is an effective treatment for malignant hyperthermia (MH). Succinylcholine and volatile anesthetic agents are potential triggers for inducing MH; however, discrepant recommendations for emergency preparedness exist regarding the availability of dantrolene during general anesthesia. The Malignant Hyperthermia Association of the United States (MHAUS) guidelines state dantrolene must be available within 10 minutes of the decision to treat MH whenever volatile agents or succinylcholine are administered.¹ In contrast, the Society of Ambulatory Anesthesia (SAMBA) Position Statement on the Use of Succinylcholine for Emergency Airway Rescue permits class B facilities to stock succinylcholine for airway rescue without dantrolene in situations where no volatile agents are used.² Larach et al. investigated whether evidence could be found to show that succinylcholine administered without volatile agents triggers MH. They also examined the relationship between dantrolene administration and MH-related morbidity and mortality.

A query of 6,368,356 anesthetic records in three databases revealed 246,904 (3.9%) cases in which succinylcholine was administered without concomitant volatile agents, in doses ranging from 0.5 to 2.5 mg/kg. A total of 24 malignant hyperthermia events were identified, 13 of which were treated with dantrolene. Fourteen patients experienced substantial complications and one died. The data lacked sufficient statistical power to show correlation between the dose of succinylcholine and triggering of MH; however, delayed administration of dantrolene resulted in markedly worsened patient outcomes. The likelihood of an MH complication increased 1.6 times for every 30-minute increase in time between the first MH sign and administration of the first dantrolene dose. The authors viewed their data as being supportive of the recommen-

dation to stock dantrolene whenever succinylcholine or volatile agents are used.

Comment: The SAMBA Position Statement on the Use of Succinylcholine for Emergency Airway Rescue, published in May 2017, noted the incidence of malignant hyperthermia to be extremely low (1.8–3.4 events per 100,000). Additionally, the authors of that position statement also were unaware of any reports of MH triggered by low-dose succinylcholine (defined as 20–30 mg), the most commonly used dosage for the treatment of perioperative laryngospasm.³ Larach et al. demonstrated that succinylcholine administered in the absence of volatile agents, over a wide dose range to manage difficult ventilation, can trigger MH events that warrant dantrolene treatment. This report shifts the consideration of succinylcholine-induced MH from the realm of highly unlikely into the realm of similarly rare but devastating emergencies, such as perioperative cardiac arrest (estimated incidence 7 per 10,000 noncardiac surgeries⁴) and anaphylaxis (estimated 1 per 10,000–20,000 anesthetics⁵). With such events, successful management depends upon the presence of well-established protocols for early recognition and prompt treatment. Dental office-based anesthesia providers also will need to consider the relatively remote nature of office-based anesthesia practice when establishing their malignant hyperthermia protocol. The average elapsed time between an emergency 911 call and arrival of paramedics to the site of the call is 7 minutes in urban and suburban areas and more than double that in rural areas.⁶ (MA Saxen)

Should Total Intravenous Anesthesia Be Used to Prevent the Occupational Waste Anesthetic Gas Exposure of Pregnant Women in Operating Rooms? Sharma A, Bhatia P, et al. *Anesth Analg.* January 2019;128(1):188–190.

Inhalational anesthetic agents are used frequently because of rapid recovery and ease of titration of their

1. The Malignant Hyperthermia Association of the United States. Available at: www.mhaus.org. Accessed January 26, 2018.

2. Joshi GP, Desai MS, Gayer S, Vila H. Succinylcholine for emergency airway rescue in class B ambulatory facilities. *Anesth Analg.* 2017;124:1447–1449.

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3. Crisis management during anesthesia: laryngospasm. Qual SJAMA Surgery October 2017 Volume 152, Number 10 9af. *Health Care.* 2005;14:e3.

4. Goswami S, Brady JE, Jordan DA, Li G. Intraoperative cardiac arrests in adults undergoing noncardiac surgery: incidence, risk factors, and survival outcomes. *Anesthesiology.* 2012;117:1018–1026.

5. Mertes PM, Tajima K, et al. Perioperative anaphylaxis. *Med Clin N Amer.* 2010;94:761–789.

6. Mell HK et al. Emergency medical services response times in rural, suburban, and urban areas. *JAMA Surg.* October; 2017;152(10):9.

alveolar concentration. However, such use is associated with the potential health hazards of waste anesthetic gases (WAGs) to the health care workers working in the operating room (OR), including pregnant women. Anesthesiologists, surgeons, nurses, and related health care workers active in the OR and the postanesthesia care unit are the workers most exposed to WAGs. The environment pollution with WAGs may be classified into three categories: anesthetic techniques, anesthesia workstation, and ORs without a volatile gas scavenging system. Improper anesthetic techniques may include poorly fitting face masks, an insufficiently inflated tracheal tube or laryngeal mask cuff, and circuit leaks. The potential health hazards of WAGs include transient problems, such as nausea, irritability, and fatigue. Long-term complications, such as teratogenic effects have an insidious onset. Prolonged exposure to WAGs can cause DNA damage in OR personnel. It also can cause impairment of the antioxidant defense system in exposed professionals. Souza et al. showed that exposure to modern WAGs resulted in genomic instability as studied by cytotoxic and proliferative changes, detected in the exfoliated buccal cells of anesthesiologists who had been exposed to WAGs for at least 2 years. Hence, they suggested that exposure of the OR personnel to these WAGs should be minimized.

Comment: The authors of this commentary, which was published in the January 2019 *Anesthesia and Analgesia*, address concerns that have been discussed in the dental literature for roughly 50 years. Beginning in 1975, Cohen et al. published survey results in the *Journal of the American Dental Association* that identified the health hazards and risks of chronic exposure to trace anesthetic gases and nitrous oxide.^{7,8} This and several subsequent studies led to the establishment of environmental exposure limits by the National Institute of Occupational Safety and Health (NIOSH), as mentioned by Sharma et al.⁹ The continued study of nitrous oxide in the dental setting helped to refine our understanding of the toxicity of nitrous oxide and best clinical practices for nitrous oxide administration.¹⁰ Readers wishing to explore this topic in depth will benefit by adding these papers to their readings. (MA Saxen)

7. Cohen EN, Brown BW et al. A survey of anesthetic health hazards among dentists. *J Am Dent Assoc.* 1975;90(6):1291–1296.

8. Cohen EN, Gift HC, Brown BW et al., Occupational disease in dentistry and chronic exposure to trace anesthetic gases. *J Am Dent Assoc.* 1980;101(1):21–31.

9. Occupational Safety and Health Administration. Anesthetic gases-guidelines for workplace exposures 1999. Available at: <https://www.osha.gov/dts/osta/anestheticgases/index.html> last accessed January 29, 2019.

10. Yagiela JA. Health hazards and nitrous oxide: a time for reappraisal. *Anesth Prog.* 38:1–11 1991.

Analysis of 17,948 Pediatric Patients Undergoing Procedural Sedation with a Combination of Intranasal Dexmedetomidine and Ketamine. Yang F, Liu Y, Yu Q et al. *Pediatr Anesth.* 2019;29:85–91

This retrospective study examined the outpatient medical records of 17,948 children presenting for diagnostic imaging studies and procedures in the Children's Hospital of Chongqing Medical University. Patients received 2 mcg/kg dexmedetomidine, and 1 mcg/kg ketamine mixed together in a 1 mL tuberculin syringe and delivered into both nostrils. Patients then were held in the supine position by parents while trained nurses massaged the ala of the nose. Sedation success was defined as successful completion of the examination with attainment of adequate diagnostic quality imaging and reports. Sedation failure was defined as the need for additional intravenous medications/inhalation agents to complete the procedure. The majority of patients were under age 5 years; 13,461 were under age 3 years. Color Doppler ultrasound, pulmonary function, and electroencephalography (EEG) accounted for 92.3% of the procedures. The average onset of sedation time was 15 minutes, while the median sedation time (defined as time from drug administration to discharge from the hospital) was 62 minutes. Major adverse events included emergency airway intervention (3%), and cardiac arrhythmias (1%), and minor adverse events included postoperative nausea and vomiting, oxygen desaturation, delayed awakening, and upper airway obstruction, all of which occurred in fewer than 1% of cases. The overall success rate was 93%. The authors concluded that this technique, when used to administer procedural sedation for nonpainful procedures, is associated with acceptable effectiveness and low rates of adverse events.

Comment: Readers should be cautious when considering the success rate and treatment times of this retrospective chart review. Cultural differences, lack of procedural detail, and selection bias limit the conclusions that can be drawn from this report. The study is noteworthy in that a large population of children underwent this well-defined, novel technique of intranasal sedation at a tertiary Chinese hospital without a significant rate of major or minor adverse effects. (MA Saxen)

Effect of Aspirin on Cardiovascular Events and Bleeding in the Healthy Elderly. McNeil J, Nelson MR, Woods RL, et al. *N Engl J Med.* 2018;379:1509–1518

Low-dose aspirin is a common therapy for secondary prevention of cardiovascular events. However, its role

in the primary prevention of cardiovascular disease is unclear. From 2010 through 2014, this prospective study enrolled community-dwelling men and women in Australia and the United States who were 70 years or older (or ≥ 65 years old among blacks and Hispanics in the United States) and did not have cardiovascular disease, dementia, or disability. Participants were assigned randomly to receive 100 mg enteric-coated aspirin or placebo. The primary end point was a composite of death, dementia, or persistent physical disability. After a median of 4.7 years of follow-up, the rate of cardiovascular disease was 10.7 events per 1000 person-years in the aspirin group and 11.3 events per 1000 person-years in the placebo group. The rate of major hemorrhage was 8.6 and 6.2 events per 1000 person-years, respectively. The authors concluded that low-dose aspirin as a primary prevention strategy in older adults resulted in a significantly higher risk of major hemorrhage and did not result in a significantly lower risk of cardiovascular disease than placebo.

Comment: Low-dose aspirin (81 mg qd) prolongs bleeding time through platelet inhibition. It often is prescribed as a preventive therapy to patients who are susceptible to the formation of emboli, such as those who have suffered from stroke, angina, or myocardial infarction. Elderly patients are at higher risk for cardiovascular events, but also are susceptible to prolonged bleeding. The risk–benefit balance for low-dose aspirin therapy in the elderly remains unknown. Based on the data from this randomized trial, the authors conclude that, for healthy elderly persons who did not have known cardiovascular disease, the use of low-dose aspirin resulted in a significantly higher risk of major hemorrhage and did not result in a significantly lower risk of cardiovascular disease than placebo. (MA Saxen)

Outpatient Opioid Prescriptions for Children and Opioid-Related Adverse Events. Chung CP, Callahan ST, Cooper WO, et al. *Pediatr.* 2018;142:e20172156.

Chung et al. examined Tennessee Medicaid records of approximately 1.4 million children and adolescents without major chronic diseases (including substance use disorder) in a retrospective cohort study that aimed to identify the frequency and indications for outpatient opioid prescriptions and associated adverse events. The largest number of opioid prescriptions in this population was provided by dentists, not physicians. The annual mean prevalence of opioid prescriptions was 15%. There were 437 cases of opioid-related adverse events, defined as an emergency department visit, hospitalization, or death. One of every 2611 opioid prescriptions was followed by an opioid-related adverse event, and three deaths were identified.

Comment: The authors report that 31.1% of all prescriptions were associated with dental procedures. For children 2 to 5 years old, 23.7% of prescriptions had an infection indication. The characteristics of opioid-related adverse events for children and adolescents 12 to 17 years old differed from those for younger children. They were more likely to result in an opioid-related intervention or escalation of care, hospitalization, or death; to involve opioids from an unidentified source; and to be related to substance use disorder or self-harm. The authors call for the development of more comprehensive pediatric guidelines for the treatment of acute, self-limited conditions. (MA Saxen)

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