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

Lodenius A, Maddison K, Lawther B, Scheinin M, Eriksson L, Eastwood P, Hillman D, Fagerlund M, Walsh J. Upper airway collapsibility during dexmedetomidine and propofol sedation in healthy volunteers. *Anesthesiology*. 2019;131(5):962–973.

Dexmedetomidine is a relatively new sedative that is promoted as having minimal effects on the ventilatory drive or the propensity for airway obstruction. However, a recent trial demonstrated impaired ventilatory drive and induction of apnea in sedated volunteers. This nonblinded, randomized crossover study examined 9 nonsmoking adults between the ages of 18 and 65 with American Society of Anesthesiologists physical status 1 or 2 and a body mass index of 37 or less. Upper airway collapsibility was measured during low and moderate infusion rates of propofol or dexmedetomidine to produce comparable levels of minimal to moderate sedation. The level of sedation was monitored with bispectral index recordings, electroencephalogram recordings, and 2 clinical sedation scales at discrete points in time and correlated with blood plasma levels of propofol or dexmedetomidine. At comparable levels of minimal and moderate sedation, both drugs produced similar degrees of pharyngeal collapsibility and reductions in ventilatory drive, suggesting that dexmedetomidine does not offer inherent protection against upper airway obstruction or ventilatory depression.

Comment: (see * below)

Weerink M, Barends C, Muskiet E, Reyntjens K, Knotnerus F, Oostra M, van Bocxlaer J, Struys M, Colin P. Pharmacodynamic interaction of remifentanil and dexmedetomidine on depth of sedation and tolerance of laryngoscopy. *Anesthesiology*. 2019;131(5):1004–1017.

Dexmedetomidine is a sedative with modest analgesic efficacy, whereas remifentanil is an opioid analgesic with modest sedative efficacy. Synergy is often observed when sedative-hypnotics are combined with opioid analgesics in anesthetic practice. A 3-phase crossover trial was conducted to study the pharmacodynamic interaction between remifentanil and dexmedetomidine. Thirty healthy volunteers, stratified by age and sex, were recruited to undergo target-controlled infusions of dexmedetomidine, remifentanil, and remifentanil with a fixed dexmedetomidine background concentration. The drug effect was measured with the Patient State Index (PSI-2), an electro-encephalograph-based depth of sedation monitor. These readings were correlated to the Modified Observers Assessment of Alertness and Sedation (MOAA/S) and serial arterial blood samples of dexmedetomidine and remifentanil. Tolerance to laryngoscopy was defined as a MOAA/S score of 0 (no response to name call, shaking or trapezius squeeze, and the ability to achieve a Cormack-Lehane grade 3 direct laryngoscopy). Despite falling asleep, most subjects remained arousable by calling their name, shaking, or delivering a trapezius squeeze. During the dexmedetomidine phase, 13 of 22 patients tolerated laryngoscopy. During the combined dexmedetomidine/remifentanil phase, 15 of 19 patients tolerated laryngoscopy. Although the addition of remifentanil slightly increased the depth of sedation and tolerance to laryngoscopy, there was no evidence of synergy, even when dexmedetomidine infusion concentrations were increased to supraclinical levels. In contrast to these findings, the addition of remifentanil to propofol creates synergy, resulting in the ability to decrease baseline propofol infusion concentrations. Dexmedetomidine potency was also observed to increase with patient age. The authors concluded that, although dexmedetomidine and remifentanil might be useful in minimal sedation, dexmedetomidine cannot be considered a suitable alternative to sedative-hypnotics for the induction of anesthesia.

Comment: (see * below)

Aouad M, Zeeni C, Al Nawwar R, Siddik-Sayyid S, Barakat H, Elias S, Yazbeck Karam V. Dexmedetomidine for improved quality of emergence from general anesthesia: a dose-finding study. *Anesthesia & Analgesia*. 2019;129(6):1504–1511.

Previously published research has suggested improved recovery scores in patients receiving intraoperative dexmedetomidine infusions; however, the efficacy of dexmedetomidine on coughing and other emergence phenomena is not consistent across studies. This prospective, multicenter, randomized, double-blind, placebo-controlled study sought to determine the optimal dose of intraoperative dexmedetomidine to prevent cough (primary outcome) and improve emergence profiles, as judged by heart rate and the absence of shivering, agitation, delayed recovery, and excessive sedation. A total of 216 adults, age 18 to 75, with American Society of Anesthesiologists physical status 1-

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3, undergoing elective surgery lasting 1 to 3 hours, were recruited for the study. The mean age for patients accepted into the study was 45 years. Participants were randomly assigned to 1 of 4 groups. At the end of surgery, patients received a single dose of either dexmedetomidine at 1, 0.5, or 0.25 mcg/kg, or a saline placebo. Following surgery, nurses blinded to the intraoperative study infusion recorded vital signs and scored cough, shivering, sedation, and postoperative nausea and vomiting at 10-minute intervals. The 1-mcg/kg dose was best for control of cough, shivering, and agitation. Dose-dependent hypotension was noted in all doses of dexmedetomidine during emergence. None of the dexmedetomidine doses delayed extubation or discharge from the Post-Anesthesia Care Unit. Limitations to this study included the lack of standardization of surgeries and a potential unintended bias due to the hemodynamic changes associated with dexmedetomidine.

*Comment: The clinical profile of dexmedetomidine continues to evolve with the appearance of new scientific reports in the anesthesia literature. Early reports on the use of dexmedetomidine demonstrated minimal or insignificant changes in ventilation when used for moderate sedation via continuous infusion without a bolus.[1] This led some to speculate that dexmedetomidine might be a better choice for minimal to moderate sedation as compared with the commonly used opioid-sedative-hypnotic combinations like fentanyl and midazolam. This report by Lodenius et al is notable in that it compared dexmedetomidine to propofol, a drug known to reduce upper airway tone.[2] Their study demonstrates the potential for airway compromise with dexmedetomidine, even when used as a single sedative drug for well-controlled moderate sedation. The relatively narrow therapeutic window, potential for hypotension, lack of a pharmacologic antagonist, and long half-life further compromises the potential use of dexmedetomidine as a drug for routine moderate sedation in dentistry.

The report by Weerink et al further characterize the use of this drug as a potential part of a drug regimen for the induction of general anesthesia and intubation. The synergy achieved by the combination of opioids with sedative-hypnotics such as propofol and barbiturates produces the deep level of consistent unresponsiveness needed to prepare patients for laryngoscopy. Prior to this study, the anesthetic literature suggested that a deep, unarousable level of unresponsiveness was achievable at high doses of dexmedetomidine. Given the potential for hazardous hypotension and bradycardia with increased doses of dexmedetomidine,[3] the combination of an opioid with a lower dose of dexmedetomidine attempted to use the principal of balanced anesthesia to lessen these undesirable effects while adding analgesia. This effect was not found, underscoring the fact that the level of sedation and sleep produced by alpha-2 agonists differs significantly from that produced by propofol. Finally, the study by Aouad and colleagues provides useful information on the use of dexmedetomidine as bolus, given by slow injection at the end of surgery. Earlier reports that described the use of dexmedetomidine as an infusion, used for sedation in the intensive care unit, were not as directly applicable the use in the office-based anesthesia setting.

Ockerman A, Bornstein MM, Leung YY, Li SK, Jacobs PR. Incidence of bleeding after minor oral surgery in patients on dual antiplatelet therapy: a systematic review and meta-analysis. *Int J Oral Maxillofac Surg*. 2020;49:90–98.

Dual antiplatelet therapy (the daily, prophylactic use of acetylsalicylic acid plus a PY2Y12 inhibitor) has become the first choice for patients with acute or stable coronary artery disease to prevent thrombotic complications. Although effective for this purpose, an elevated risk of bleeding has been observed in patients receiving dual antiplatelet therapy and undergoing minor oral surgery such as extractions, dentoalveolar surgery, cyst removal, and periodontal treatment. Some surgeons have considered suspending dual antiplatelet therapy to improve perioperative hemorrhage control; however, withdrawal of dual antiplatelet therapy may result in serious systemic adverse events. This systematic review of 16 published studies examined the risk of bleeding in this population as compared with oral surgery patients receiving single antiplatelet or no antiplatelet therapy. Although dual antiplatelet therapy was associated with significantly greater perioperative bleeding, all studies confirmed that local hemostatic measures were adequate in stopping bleeding. Considering these findings, the interruption of dual antiplatelet therapy prior to minor oral surgery is not recommended.

Comment: The recommendation to maintain antiplatelet therapy in patients undergoing minor oral surgery is consistent with the recently published findings of the World Workshop on Oral Medicine VII, which examined studies of patients placed on direct oral anticoagulant drugs.[4] That review and analysis noted that all postoperative bleeding events were controlled with local measures and found no important differences in postoperative bleeding when comparing patients who had discontinued antiplatelet therapy to those who maintained it. In contrast to this, there was little for the

anesthesiologist on whether to employ nasal intubation versus an alternative form of airway management in this set of patients.

Echeverria-Villalobos M, Todeschini A, Stoicea N, Fiorda-Diaz J, Weaver T, Bergese S. Perioperative care of cannabis users: a comprehensive review of pharmacological and anesthetic considerations. *J Clin Anesthesia*. 2019;57:41–49.

According to the 2015 National Survey on Drug Use and Health, marijuana continues to be the most common illicit recreational drug in the United States. Cannabinoids have multisystem effects that can interfere with anesthetic agents and lead to serious consequences. This comprehensive review examines the main physiological effects of cannabinoids and their interactions with common anesthetic drugs.

All summaries and comments provided by

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1. Ebert TJ, Hall Je, Barney JA, et al The effects of increasing plasma concentrations of dexmedetomidine in humans. *Anesthesiology*. 2000;93:382–394.

2. Eastwood PR, Platt PR, Shepherd K, et al Collapsibility of the upper airway at different concentrations of propofol anesthesia. *Anesthesiology*. 2005;103(3):470–477.

3. Gerlach AT, Dasta JF. Dexmedetomidine: an updated review. *Ann Pharmacother*. 2007;41(2):245–252.

4. Manfredi M, Dave B, Percundani D, et al. World workshop on oral medicine VII: direct anticoagulant agents management for invasive intraoral procedures: a systematic review and meta-analysis. *Oral Dis*. 2019;25(Suppl 1):157–173.