Tooth Technician or Oral Health Doctor?

Scrubs was a favorite television show of mine during dental school and residency. In one memorable scene, the irascible well-seasoned chief of staff Dr Kelso says, while chiding a particularly poor performing intern, "Is that how you feel, future dentist?" Although I found it hilarious, a fellow classmate was quite offended and declared it patently unfunny considering dentists are doctors too. Dentistry is more than being a tooth technician; it is being a doctor of oral health (ie, the mouth and facial regions) and even the head and neck in the case of the specialty of orofacial pain. But therein lies the rub. Better walk the walk if you talk the talk. The necessity of properly assessing and understanding a patient's medical status is rightly emphasized in dental education. It is not something to be cavalierly glossed over due to mounting production pressures, yet from time to time that unfortunately seems to be the case.

In the April 2022 issue of the *Journal of the American Dental Association*, survey data obtained from 258 members of the American Dental Association Clinical Evaluators Panel detailed how practicing dentists use and access patient health information.[1] Stated objectives included understanding how dentists assess their patient's health status, how frequently this information is updated, and how dentists interact with medical colleagues. The American Dental Association Clinical Evaluators Panel is "used to take the pulse of ADA member perceptions and feedback regarding professional products, materials, and clinical techniques." Based on the demographic data, respondents closely approximated recently published American Dental Association dentist workforce statistics with respect to sex, geographic region, and race/ethnicity, although the mean respondent age was slightly higher than average (55 years vs 49.3 years).[2,3] Additionally, 84.9% of respondents reported being in general practice, while 15.4% practice a dental specialty.

Many of the clinical insights from the study include aspects of patient care that most would consider well established and generally known. For example, vital signs are collected, medical histories and medication lists updated, and medically compromised patients are treated, all with regularity. The authors note that dentists do interact closely with other physicians, particularly for patients with medical complexities. Those findings appear to be on par with dentistry upon initial examination.

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However, diving deeper into the article's infographic revealed several eyebrow-raising datapoints. According to the survey, the person who discussed/reviewed a new patient's medical history was the dentist 60% of the time, followed by the dental hygienist (19%), dental assistant (17%), and other (4%). In comparison, the person who discussed/reviewed medical history for returning patients was primarily the dental assistant (34%) or dental hygienist (32%), followed by the dentist (21%), and other (13%), of which a third identified as being front-office staff or the office manager.

Knowing your patient is fundamental to safe patient care and medical emergency prevention. A health history review (medical history, review of systems, medication list, etc) should be one of the first steps completed for all dental patients, not just those undergoing sedation or general anesthesia. Starting with the form completed by the patient, the health history review ideally includes initial assessment by and verbal interview with the treating dentist, and it should be concisely reviewed at each return visit. Building intended redundancy into the process by having a subordinate prescreen patients can be quite helpful; however, it should not be delegated in its entirety. Putting aside dental hygienists with their potential to work independently, the percentage of dentists who discuss/review health histories for new and returning visits should be 100% rather than 60% and 21%, respectively. Especially worrisome is the significant percentage delegating this critical step to "others" who likely lack the same level of medical education as the treating dentist or dental hygienist.

The infographic also shed light on the type of information obtained and recorded at every dental visit, with a majority updating changes to medical history (75%) and the medication list (66%), while a minority included visits with other health care providers (33%). Although it is commendable that more than half stated patients are asked about medical history and medication updates at every visit, the outliers highlight further room for improvement.

Treating patients without a full picture of their current health history considerably elevates the potential for patient harm and medical-legal risks. Patients should be asked if any changes to their medical history or listed medications have occurred since their last visit. Inquiring about any significant visits with other health care providers is also appropriate as potential pitfalls may be discovered preoperatively. This line of questioning is easily completed and takes virtually no time. If delegated, notable findings can be easily relayed to the dentist for further discussion prior to starting treatment.

Furthermore, it is generally advisable to consider taking an entirely new health history at regular intervals (eg, every 2–3 years) to help ensure any major changes are not inadvertently missed.

Lastly, a large majority (85%) reported routinely collecting some combination of vital signs (pulse, blood pressure, respiratory rate, room air oxygen saturation, or temperature) upon presentation, and 57% of those respondents stated they collect those same vitals at every visit. The 15% of outliers who do not routinely collect vital signs upon the patient's arrival are particularly troubling. The survey data fail to discuss any particular combinations, however; blood pressure is probably the most likely, and hopefully heart rate as well, and both would certainly be indicated for any dental patient undergoing treatment requiring local anesthesia, particularly with added epinephrine, let alone sedation or general anesthesia. Assessing a patient's respiratory rate, oxygen saturation, or temperature may be unneeded for otherwise healthy patients undergoing routine dental care. However, some notable exceptions come to mind where their use would be clearly indicated: a patient with significant pulmonary disease, those taking medications that may depress the central nervous system, signs and symptoms suggestive of a systemic or serious odontogenic infection, or perhaps even suspected opioid use.

Obtaining baseline vital signs is a commonly delegated task performed in many offices. They can be taken immediately upon the patient's entry into the dental operatory and the findings, normal or otherwise, easily relayed to the treating dentist with little to no delay in treatment. Given the widespread incidence of cardiovascular disease and hypertension in the United States, it is quite shocking that only a little more than half of all respondents take vital signs at each visit, although those who do should be commended. Identifying irregularities preoperatively is one key to preventing perioperative medical emergencies and urgencies in the dental office but obviously requires vital signs are actually assessed prior to treatment.

While this survey did identify some bright spots for dentistry, it also seemingly underscored several areas of concern. Clearly there is room for improvement with respect to who discusses/reviews patient health histories, when health information is updated, and obtaining appropriate vital signs. All dentists must ensure they are working with a thorough and up-to-date medical history for every patient, regardless of whether the planned treatment includes noninvasive care only or local anesthesia, sedation, or general anesthesia. This cornerstone of care is critical to serving as our patient's oral health doctor rather than their tooth technician.

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Optimal Timing of Intravenous Acetaminophen Administration for Postoperative Analgesia

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Objective: Acetaminophen (APAP) is widely used as an analgesic for postoperative pain relief. However, the pharmacokinetic-pharmacodynamic (PK-PD) properties of intravenous APAP administration remain unclear. We developed a PK-PD model in adult volunteers.

Methods: APAP (1 g) was intravenously administered to 15 healthy volunteers. The pain equivalent current (PEC) was then measured using the pulse current, corresponding to the quantitative value of pain perception. The PK model was developed using a 2-compartment model, and the PD model was developed using a linear model and an effect compartment model.

Results: APAP plasma concentration peaked just administration, whereas PEC significantly increased at 90 minutes and lasted through the experimental period (300 minutes). APAP plasma concentrations and PEC were processed for use in the PK-PD model. The developed PK-PD model delineates the analgesic effect profile, which peaked at 188 minutes and lasted until 327 minutes.

Conclusion: We developed the PK/PD model for APAP administered intravenously. The analgesic effect can be expected ~90 minutes after administration and to last >5 hours. It is suggested that APAP be administered ~90 minutes prior to the onset of anticipated postoperative pain.

Key Words: Acetaminophen; Postoperative pain; Pharmacokinetic-pharmacodynamic model; Intravenous.

Acetaminophen (APAP) is an analgesic that is widely used to relieve postoperative pain. APAP is thought to act as a substrate for the peroxidase activity of cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) and to exert its anti-inflammatory and analgesic effects by decreasing prostaglandin H2 through competition with prostaglandin G2.[1] Furthermore, the similarity of its in vivo action to that of selective COX-2 inhibitors has been confirmed.[2,3] Although APAP was originally thought to act peripherally, accumulating data now support an analgesia effect on the central nervous system (CNS). APAP is now thought to stimulate serotonergic pathways involved in pain inhibition,[4] activate cannabinoid receptors indirectly, and have activity on NMDA and substance P receptors in the spinal cord.[5,6]

The antipyretic effect of APAP reportedly occurs 2 hours after its peak plasma concentration has been reached.[7] The analgesic effect of APAP can also be delayed for 1 to 2 hours after administration even though peak plasma concentration is observed just after administration.[8,9] Thus, the plasma concentration is not considered to be an effect site. This hypothesis is supported by the measurement of APAP concentrations in cerebrospinal fluid after intravenous (IV) administration in children and adults.[10,11] Based on these findings, the administration of APAP 1 to 2 hours before anticipated pain and fever has been recommended in children.[12] Although the early administration of APAP is recommended for the purpose of postoperative analgesia, pharmacokinetic and pharmacodynamic studies of APAP and its exerted effect on postoperative pain are rare. The available pharmacokinetic-pharmacodynamic (PK-PD) models for APAP have been developed mainly for oral administration in chil-

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dren.[7,12,13] The PK-PD model for IV administration in adults has not yet been explored.

The intraoperative use of APAP is left to the discretion of each anesthetist. APAP might not be optimally administered because an effective regimen for APAP has not yet been proposed. Determining the optimal timing of APAP administration could provide valuable information for evaluating the potency of APAP against postoperative pain and could help to reduce opioid use for postoperative analgesia. An adjuvant to opioids for postoperative pain relief is eagerly awaited to avoid the various adverse effects of opioid use and delay in hospital discharge.

We investigated the PK-PD profile of APAP in volunteers and examined the relationship between the PK-PD profile and the effect of APAP on pain perception.

METHODS

Ethics and Study Design

This study was approved by the Showa University Clinical Research Review Board (approval number: CRB3200002) and was registered at jRCT (https://jrct.niph.go.jp; registration number: jRCTs031200321, Akiko Nishimura, January 21, 2021).

The study design was a randomized, single-blinded, crossover trial comparing IV APAP (Acelio Intravenous Injection, 1000 mg/100 mL bag, Terumo Corp) and a saline placebo. This study was conducted at Showa University Clinical Institute for Clinical Pharmacology and Therapeutics (Tokyo, Japan), from January 21, 2021, to March 9, 2021. The testing period was 2 days followed by a 1-week washout period. After obtaining informed consent, the institute staff registered study participants using an identification code for anonymization and random allocation to 1 of 2 groups. Participants were divided according to sex and then randomly assigned in a 1:1 ratio to receive either APAP or saline on the first day of testing; the randomization was performed using a random number table without stratification. Subjects' height, weight, and vital signs were measured. A cannula was inserted in the dominant arm for blood sampling and in the nondominant arm for drug administration. In total, 1000 mg of APAP or an equivalent volume of saline placebo was intravenously infused for 15 minutes using an infusion pump. Vital signs were measured at 60, 120, and 240 minutes after administration. The analgesic effect and the plasma APAP concentration were also evaluated.

Subjects

Fifteen subjects aged 20 to 60 years with an American Society of Anesthesiologists (ASA) physical status of I were enrolled. All subjects provided written informed consent. The exclusion criteria included a known allergy to APAP; peptic ulcer disease; serious blood coagulation disorders; serious liver, renal, or cardiac dysfunction; aspirin-induced asthma; pregnancy or breastfeeding; the presence of an electronic implant; or any medical concerns that might impact the study.

Evaluation of Analgesic Effect and Plasma Concentration

We used the PainVision PS-2100 device (Nipro Corp) to evaluate analgesia. The PainVision device was developed to evaluate pain and sensory perception quantitatively and can be used to evaluate the effects of treatment and medication.[14–16] This device selectively stimulates Aβ and Aδ sensory fibers by sending pulses of electric current along the surface of the body and then records the participant's sensory threshold. The electrode is attached to the ulnar side of the forearm opposite the dominant hand, and the subject holds a hand switch in the other hand. The subject then presses the hand switch when he or she perceives a current or feels pain. The current perception threshold (CPT) was defined as the minimum current that could be perceived by the subject. The pain equivalent current (PEC) was defined as the current at which the subject first felt pain. The CPT and PEC were obtained before APAP administration (PRE values) and at 0, 30, 60, 90, 120, 180, 240, and 300 minutes after administration.

Parameters were each measured 3 times with different current rise times to prevent the subject from becoming acclimated (CPT: 60, 80, and 100 seconds; PEC: 30, 40, and 50 seconds). When outliers appeared, the parameter was remeasured using the same current rise time; a maximum of 3 remeasurements were allowed. The closest 3 values were averaged. The change in each value relative to the PRE value was calculated and used for analysis. The subjects practiced before the actual measurement. We used the PEC value as the pain threshold, which was considered to reflect the intensity of the analgesic effect of APAP. In this manner, the PEC values were used in the PK-PD study modeling as a value reflecting the pharmacological target effect of APAP.

Blood samples (5 mL) were obtained before APAP administration (PRE) and at 0, 15, 30, 45, 60, 90, 120, 180, 240, and 300 minutes after administration. The blood samples were collected into vacuum tubes, and the

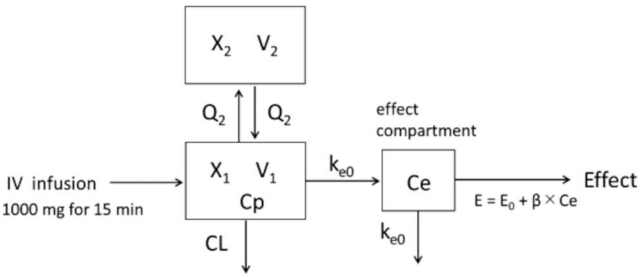

Figure 1. Schematic structure of the pharmacokinetic-pharmacodynamic (PK-PD) model. Drug administered into and eliminated from a central compartment: X_1 and X_2 are drug amounts in the central and peripheral compartments, and V_1 and V_2 are distribution volumes of the central or peripheral compartments, respectively; Cp is the plasma drug concentration. CL is the clearance from the central compartment, and Q_2 is the intercompartmental clearance. The central compartment is connected to an effect compartment by a first-order equilibration rate constant: Ce is the drug concentration in the effect compartment. The k_{e0} parameter describes the equilibration rate constant between the central compartment and the effect compartment.

plasma was separated by centrifugation at 1520 × g for 10 minutes. The plasma samples were refrigerated until analysis. The human plasma concentrations of APAP were measured using an enzyme immunoassay (EIA) method and the Clinical Chemistry Automatic Analyzer Cobas 6000 (Roche Diagnostics KK) at BML Inc (Tokyo, Japan).

PK-PD Modeling

The PK-PD analysis was performed based on the time profiles of the plasma APAP concentrations and the analgesic effects after the IV infusion of APAP (1 g) to 15 healthy subjects. A PK-PD model incorporating an effect compartment was constructed using Phoenix WinNonlin 8.3 software (Certara; Figure 1), and the model parameters for each subject were estimated.

The PK profile of APAP was also analyzed using a linear 2-compartment model. APAP was infused intravenously into the central compartment for 15 minutes, and the time profile of the plasma APAP concentration (Cp) for each subject was fitted to the above PK model. The PK-related parameters in the model were estimated for each subject and consisted of the distribution volume of the central compartment (V_1), the distribution volume of the peripheral compartment (V_2), the total clearance (CL), and the intercompartmental clearance (Q_2). In addition, the volume of distribution (V_d) and the elimination half-life ($T_{1/2}$) were calculated as secondary PK parameters using the estimated parameters.

The rate of change in PEC was used as the analgesic effect. By incorporating the effect compartment with a first-order equilibration rate constant (k_{e0}) into the PK model, the delay in the effect was described.[17] The APAP concentrations in the effect compartment and the rate constant between the central compartment and the effect compartment were represented as Ce and k_{e0}, respectively. The rate of change in Ce ($\frac{dCe}{dt}$) was defined using k_{e0} according to the following previously reported equation.[18]

$$\frac{dCe}{dt} = k_{e0} \times (Cp - Ce)$$

Regarding the PD model connected to Ce, a linear effect model was used to describe the PD of AAP as follows:

$$E = E_0 + \beta \times Ce$$

where E is the effect, E_0 represents the effect at baseline (PRE; set at 0 in this study), and β is a proportional constant of the linear relationship between the APAP concentrations in the effect compartment and the analgesic effect, or the rate of PEC change. The PD model parameters (k_{e0} and β) were estimated for each subject by applying the observed time-effect profile to the PK-PD model with the estimates obtained in the above-described PK analysis. All fitting procedures were performed using a nonlinear least square method and Phoenix WinNonlin software.

Statistical Analysis

The data obtained were analyzed using JMP clinical 6.1 (SAS Institute Inc). All data were reported as the mean ± SD or number of subjects. Continuous data were checked for equality of variance using the Shapiro-Wilk test, and nonparametric data were reported as the median (interquartile range). A P value of < 0.05 was considered to indicate statistical significance.

The differences between the APAP and control groups were tested using a multivariate analysis of variance (MANOVA). A Kruskal-Wallis test was used for the statistical analysis for the intragroup difference in the PEC values in the APAP and control groups. A Dunn post-hoc test of multiple comparisons was used to determine whether a significant difference existed at each time point if a significant difference was first indicated using a Kruskal-Wallis test.

Sample Size Calculation. Although no previous studies have verified the analgesic effect of acetaminophen using the PainVision device, 1 article in Japanese examining the analgesic effect of NSAIDs using the

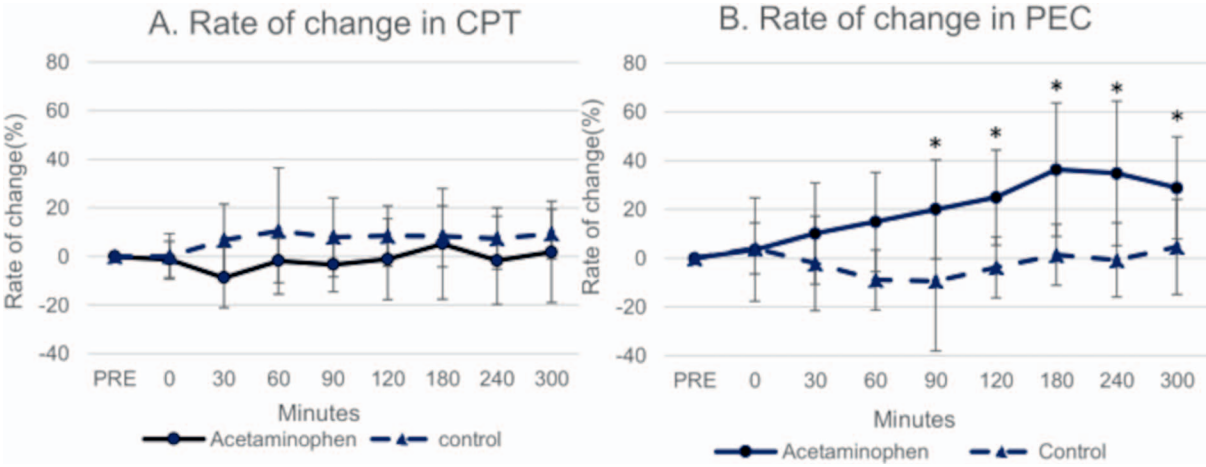

Figure 2. Rate of change in current perception threshold (CPT) (A) and pain equivalent current (PEC) (B) in the acetaminophen (APAP) and control groups.No significant difference in the rate of CPT change was seen between the APAP and control groups (Figure 1A). On the other hand, the rate of PEC change was significantly higher in the APAP group than in the control group, and the PEC in the APAP group differed significantly at time points between 90 and 300 minutes compared with the PRE value (Figure 1B).* $P < .05$ (vs PRE value).

CPT obtained using PainVision (data not shown) has been reported This previous report was used to determine an appropriate sample size. An a priori power analysis showed that 6 patients were required to detect a difference at a power of 80% using a 2-sided significance level of .05. Although no previous reports have examined the analgesic effect using PEC, 1 study showed that the rate of change in PEC was larger than the rate of change in CPT.[19] The sample size was estimated using a *t*-test and a χ^2 test with G* power software version 3.1.9.2.

RESULTS

A total of 16 subjects were scheduled to participate, but 1 subject withdrew. An additional subject was not enrolled because a post-hoc power analysis resulted in a value of 98.6% at a .05 level of significance. The background characteristics of the 15 subjects were as follows: age 29 ± 3 years; sex (M/F) 7/8; height 165 ± 10 cm; and weight 58.3 ± 8.3 kg. All subjects met the eligibility criteria, and the BMI range was from 17 to 26 kg/m^2. None of the subjects experienced an adverse event, and all the subjects exhibited normal vital signs.

In both groups, the CPT remained unchanged throughout the experimental period (Figure 2A). The PEC in the APAP group was significantly higher than that in the control group throughout the experimental period. No significant difference in PEC was observed between the PRE and 300-minute time points in the control group, but a significant difference was observed in the APAP group. Compared with the PRE value, the PEC in the APAP group differed significantly at time points between 90 and 300 minutes after APAP administration, suggesting that the onset of the analgesic effect occurred 90 minutes after administration (Figure 2B).

The plasma concentration peaked just after APAP administration, whereas the PEC peaked 180 minutes after administration (Figure 3). Thus, a substantial significant time lag, as high as 180 minutes, was confirmed between the peak plasma concentration and the peak analgesic effect.

The PK of IV APAP was described using a 2-compartment model (Figure 1). The PK-PD parameter estimates for the plasma concentration and pharmacological analgesic effect of APAP derived using the plasma concentration and the PEC of the 15 subjects, respectively (Figure 3), are shown in the Table. The fitted time-concentration/effect profiles are delineated (Figure 4), the descending slope were slower than the ascending slope. According to this PK-PD model, the effect reached the peak at 188 minutes, then gradually decreased. It is estimated from this model that the time that reached the corresponding value on the ascending slope at 90 minutes was at 327 minutes on the descending slope (Figure 4).

DISCUSSION

APAP has been recommended for use as an adjuvant to opioids in practice guidelines for acute pain management in perioperative settings published by the ASA in 2012. These guidelines state that "the ASA members

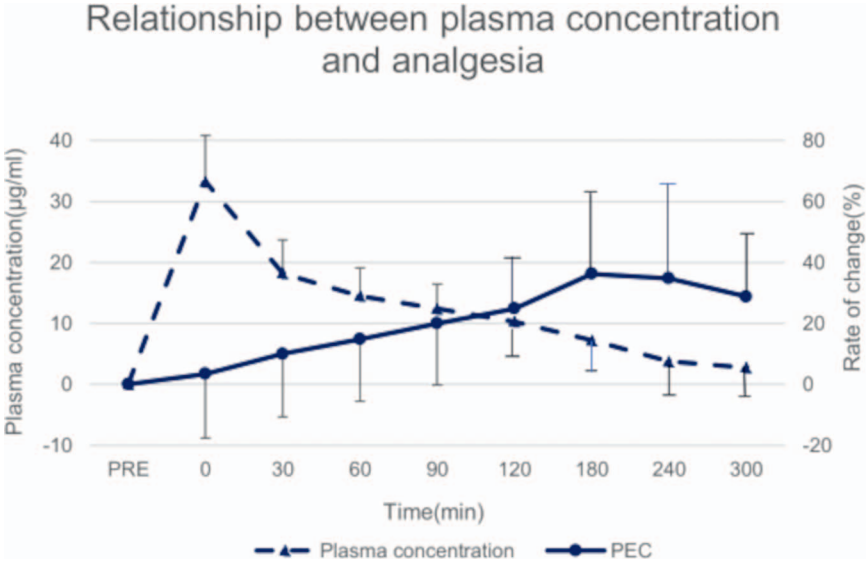

Figure 3. Relationship between plasma acetaminophen (APAP) concentration and pain equivalent current (PEC) value (Figure 2B).The plasma APAP concentration reached its highest level immediately after administration, but the analgesic effect peaked at 180 minutes after administration. Note that the target effect was substantially delayed after the peak of the plasma concentration.

agree and the consultants strongly agree that acetaminophen should be considered as part of a postoperative multimodal pain management regimen".[20] Although the efficacy of APAP as an alternative analgesic for postoperative pain has been recognized, the optimal utilization of APAP has yet to be determined. Most studies recommend around-the-clock administration every 4 to 6 hours.[21–23] However, timing for the optimal administration of IV APAP to target the peak of postoperative pain yet to be reported.

The onset of APAP's efficacy has been shown to be 1 or 2 hours, which is relatively late.[24] The delay in the analgesic effect of APAP was first confirmed in relation to its use as an antipyretic. Kelley et al[7] reported that body temperature decreased 2 hours after the peak plasma concentration had been reached. This unique property of APAP suggests a central action. APAP has been confirmed to exert its analgesic effect by acting on receptors involving NMDA and substance P in the spinal cord.[25,26] The cerebrospinal concentrations of APAP have been measured in both children[10] and adults.[11] Because of these studies examining the effect of APAP on the central nervous system, we were motivated to confirm the time-course of the analgesic effect of APAP and whether the analgesic effect corresponded with the pharmacokinetic properties associated with the cerebrospinal concentration.

PK-PD models of APAP have been previously studied in children,[12,13] since APAP has been mainly used as an antipyretic for children and as an alternative to NSAIDs. PK-PD studies in adults have been rare. APAP has been mainly used as an oral medication; thus, most PK-PD models in adults have been proposed for oral administration.[27] To the best of our knowledge, our proposed model for IV APAP use in adults is therefore quite unique. An advantage and novel point of our PK-PD model was that it was based on the pain perception of patients, and not the effect site concentration of the agent. Therefore, we think that our model was able to explain the clinical manifestations of the analgesic effect of APAP.

The PK parameters such as clearance and distribution volume that were obtained in the present study

PK-PD Parameters Estimated in Healthy Adults*

Parameters	*Mean (n = 15)*	*SE*
Estimates		
PK		
V_1 (L)	22.42	1.90
V_2 (L)	21.86	3.82
CL (L/hr)	15.74	1.64
Q_2 (L/hr)	55.70	8.14
PD		
K_{e0} (hr^{-1})	0.248	0.017
E_0	0 (fixed)	—
β	0.044	0.010
PK secondary parameters		
V_d (L)	44.27	3.39
$T_{1/2}$ (hr)	2.09	0.14

* CL, total clearance; E_0, effect at baseline; k_{e0}, first-order equilibration rate constant; PK-PD, pharmacokinetic-pharmacodynamic; Q_2, intercompartmental clearance; SE, standard error; $T_{1/2}$, elimination half-life; V_1, distribution volume of the central compartment; V_2, distribution volume of the peripheral compartment; V_d, volume of distribution.

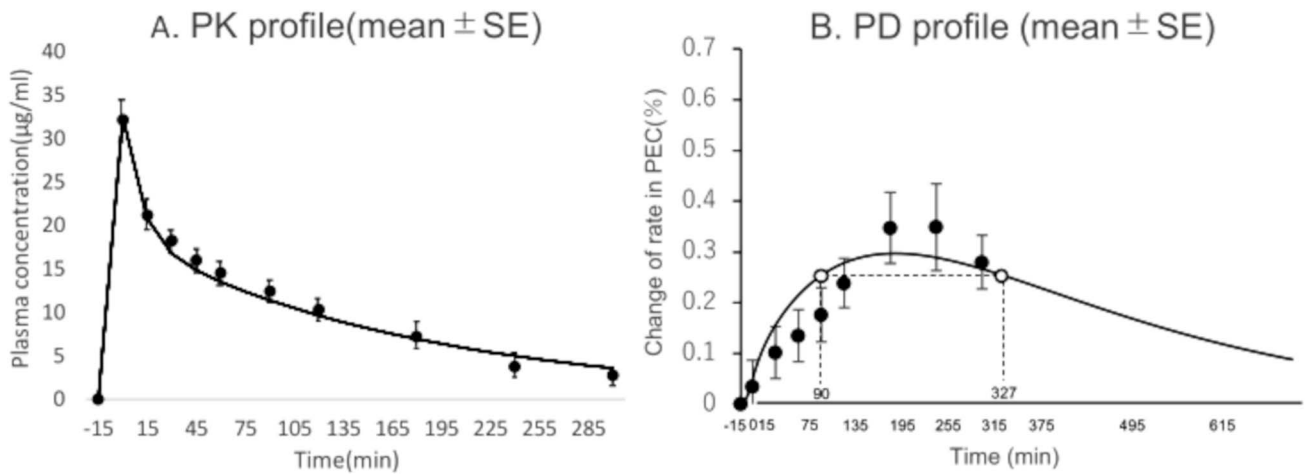

Figure 4. The pharmacokinetic-pharmacodynamic (PK-PD) model developed using the acetaminophen (APAP) plasma concentration and pain equivalent current (PEC) data.The PK model (A) was developed using a 2-compartment model, and PD model (B) was developed using a linear model and an effect compartment model. The symbols represent the mean and standard error (SE) that were obtained in 15 subjects. Open circles and the dashed line represent the duration of the analgesic effect of APAP estimated by PK-PD model.

were comparable with previously reported values.[28–30] The $t_{1/2}$ was ~2 hours, indicating the prompt elimination of APAP from the plasma. A counterclockwise hysteresis was observed between the APAP plasma concentrations and the effect (ie, the rate of change in PEC), suggesting the delayed onset of the analgesic effect. Therefore, the effect compartment was incorporated into the model to express the delayed drug action mathematically. Previous reports also suggest that the analgesic effect of APAP is correlated with its concentration at the effect site rather than its plasma concentration.[10,11,27] Some previous reports[24,27] used the sigmoid Emax model to describe the relationship between the APAP concentration in the effect compartment (Ce) and the effect (E). However, in this study, a linear model was used for the PK-PD relationship, since a saturation phase of the effect was not apparent and analyses using an Emax model or a log-linear model did not provide a reliable convergence of PD parameters. The population PK model formulas for APAP reported by Würthwein et al[28] include body weight as a covariate, and Imaizumi et al[29] reported that these formulas also described the pharmacokinetics of APAP in Japanese patients undergoing elective surgery. In addition, Allegaert et al[30] reported that size (ie, total body weight and fat free mass) and age are important covariates for APAP pharmacokinetics to explain the variabilities of clearance and distribution volume variability in adults, including healthy volunteers. The ages of the healthy adults and the patients in this study were within the same range; therefore, a simulation based on the standardization of PK parameters according to body weight would be appropriate.

We utilized the PainVision device to evaluate pain quantitatively. This apparatus delivers a pulsed current with a pulse width of 0.3 milliseconds and a pulse frequency of 50 hertz; the intensity of the current was controllable. The CPT and PEC parameters were then used to quantitate the thresholds of sensory perception and pain perception, respectively. The latter parameter was then confirmed using the VAS score.[31] The intensity of pain perception can be quantitatively evaluated by the pain generated by a current. Subjects are asked to push a button when they feel pain. The PainVision is a useful means of quantitative assessing pain in healthy subjects without chronic pain.[31,32] We considered the pain thresholds to reflect the analgesic effect of APAP.

We demonstrated that the analgesic effect of IV APAP can be expected ~90 minutes after administration in adults, and its effect lasts longer than 5 hours. Planned continuous maintenance of APAP medication based on the PK/PD model should result in an optimal administration regimen and could reduce the unnecessary or excessive use of NSAIDs and opioids for postoperative pain management.

CONCLUSION

The developed PK-PD model of IV APAP suggests the appropriate timing for administration to maximize postoperative analgesia. At least 90 minutes is required to achieve the analgesic effect of IV APAP.

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A Comparison of Two Stool Positions for Stabilizing a Dental Chair During CPR

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Objective: Most dental chairs lack sufficient stability to perform effective manual chest compression (MCC) during cardiopulmonary resuscitation (CPR). A stabilizing stool can significantly reduce backrest vertical displacement in all chair types; however, a severely curved exterior backrest may negatively impact the stool's effectiveness. This study evaluated the efficacy of 2 stool positions for stabilizing a dental chair during MCC.

Methods: Chest compressions were performed on a manikin positioned in a dental chair while vertical displacement of the chair backrest during MCC was recorded using video and measured. Vertical displacement data were captured with no stool and with a stabilizing stool in 2 different positions. Reduction ratios were calculated to evaluate the effectiveness of the 2 stool positions.

Results: With no stool, the backrest median (interquartile range) vertical displacement during chest compressions was 16.5 (2.5) mm as compared with 12.0 (1.5) mm for the stabilizing stool positioned under the area of MCC and 8.5 (1.0) mm under the shoulders. The stool positioned under the shoulders produced a significantly increased calculated reduction ratio of 48% (14%) compared with 27% (20%) under the area of MCC ($P < .001$).

Conclusions: Positioning a stabilizing stool under the shoulders was more effective at reducing vertical displacement of the dental chair backrest during chest compressions than positioning the stool under the area of MCC.

Key Words: Cardiopulmonary resuscitation (CPR); Manual chest compression (MCC); Dental chair; Stool position; Dental surgery.

The usefulness of stabilizing dental chairs with a stool for effective manual chest compression (MCC) during cardiopulmonary resuscitation (CPR) has been previously reported.[1,2] This technique utilizes a dental chair lowered to contact a stool placed under the reclined or horizontal backrest to provide additional support. This technique was adopted in the 2015 and 2021 European Resuscitation Council (ERC) Guidelines.[3,4] We previously investigated the usefulness of stabilizing stool placed just under the area of MCC in 8 different types of dental chairs and found the stabilizing stool significantly reduced backrest vertical displacement in all chair types. However, it was noted that the efficacy of a stabilizing stool was very low for a dental chair with a severely curved backrest exterior.[5] Dental chair backrest shapes can vary considerably, and in chairs with severely curved exteriors, the contact area of the stool could differ and alter its stabilizing effectiveness during MCC.

The objective of this study was to compare the efficacy of 2 stool positions for stabilizing the same dental chair with a severely curved backrest exterior from our previous study during MCC.[5] Chest compressions were performed without a stabilizing stool to establish a baseline and then repeated with the stool placed either under the area of MCC or under the shoulders. Vertical displacement measurements during compressions were recorded and the calculated reduction ratios of the 2 stool positions compared. We hypothesized that positioning the stabilizing stool under the shoulders would have an increased reduction ratio indicating increased effectiveness and reduced vertical

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displacement during chest compressions as compared with the stool positioned under the area of MCC.

METHODS

The dental chair (EOMαII; GC) with the severely curved exterior was used throughout this study. The following 3 health care providers, who all completed a certified American Heart Association (AHA) course in Basic Life Support, participated in this study: (A) 47-year-old male, 175 cm, 93 kg; (B) 44-year-old male, 177 cm, 60 kg; (C) 44-year-old female, 157 cm, 50 kg. Each study participant individually performed 10 contiguous rounds of MCC (20 compressions per round; 200 compressions total) at a pace of 100 compressions per minute in synchrony with a metronome for each of the 3 stool configurations (ie, under MCC area, under shoulders, or no stool). A total of 600 chest compressions 5.1 to 6.0 cm in depth were recorded per participant.

The study procedure was performed according to a previously established method in which the CPR manikin (Resusci Anne Torso Basic version 2011; Laerdal Medical AS) was positioned on the reclined dental chair with the upper end of the manikin torso aligned with the top edge of the backrest (Figure 1A; red line). The superior surface of the backrest under the lower half of the manikin's sternum was positioned horizontally using a levelling instrument. The hand position for MCC was the center of the chest (Figure 1B). A metal indicator (point P) was secured to the inferior surface of the dental chair directly under the area for MCC and made parallel to the floor with a level gauge. The distance of point P relative to the inferior surface of the backrest remained fixed for the duration of the study (Figure 2). Displacement of point P was captured using video recordings and measured while each health care provider performed MCC on the resuscitation manikin. MCC depth was kept between 5.1 and 6.0 cm during the study. The actual MCC depth was evaluated with the manikin's SkillReporter system, which has green lights indicating compression depths of 5.1 to 6.0 cm (Figure 2C). Any compressions outside of that range (ie, no green lights) were excluded. When compression depths were within 5.1 to 6.0 cm, the vertical displacement of the backrest from its initial position was recorded and included for analysis. Video data were transferred to a computer, and the backrest vertical displacement measurements were determined using the simultaneously captured ruler for reference.

The stabilizing stool placed under the backrest of the dental chair for this study was round with a hard seating surface (diameter 30 cm; height 45 cm; FB-01ALLBK, Fuji Boeki Co, Ltd). The superficial edge of the stool's seat was set to vertically contact the backrest either just under the area for MCC or under the shoulders (Figure 1).

Statistical Analysis

The programming language R (version 4.0.2; The Comprehensive R Archive Network) was used for statistical analysis. Vertical displacement measurements (maximum distance of point P from baseline during MCC) for the 3 participants were combined and analyzed separately at each of the 3 positional configurations. The change in vertical displacement for each of the 2 stool positions compared with baseline (ie, no stool) was calculated using the following equation:

reduction ratio = 1 – (displacement with stool/displacement without stool).

Data sets were analyzed using the Shapiro-Wilk test to determine normality of distribution. The nonparametric data sets were then analyzed using the Wilcoxon rank sum test to determine statistical significance ($P < .05$).

RESULTS

The vertical displacements of the dental chair backrest induced by MCC were assessed without and with the use of a stabilizing stool (placed under MCC or under the shoulders). A total of 1800 MCCs were recorded, but 6 were ultimately excluded due to inappropriate compression depth or an unclear recording.

Use of a stabilizing stool positioned either under the area of MCC or under the shoulders decreased backrest vertical displacement during MCC compared with no stool for all 3 participants (Table; Figure 3). Positioning the stabilizing stool under the shoulders significantly increased the calculated reduction ratio by 21% compared with placing the stool under the area of MCC (48% vs 27%; $P < .001$; Table).

DISCUSSION

In this study, the efficacy of a stool positioned as a stabilizer during CPR was investigated using a dental chair with a severely curved backrest exterior. This is the first report to our knowledge that compares the stabilizing support provided by a stool in 2 different positions when used to reinforce a dental chair with a

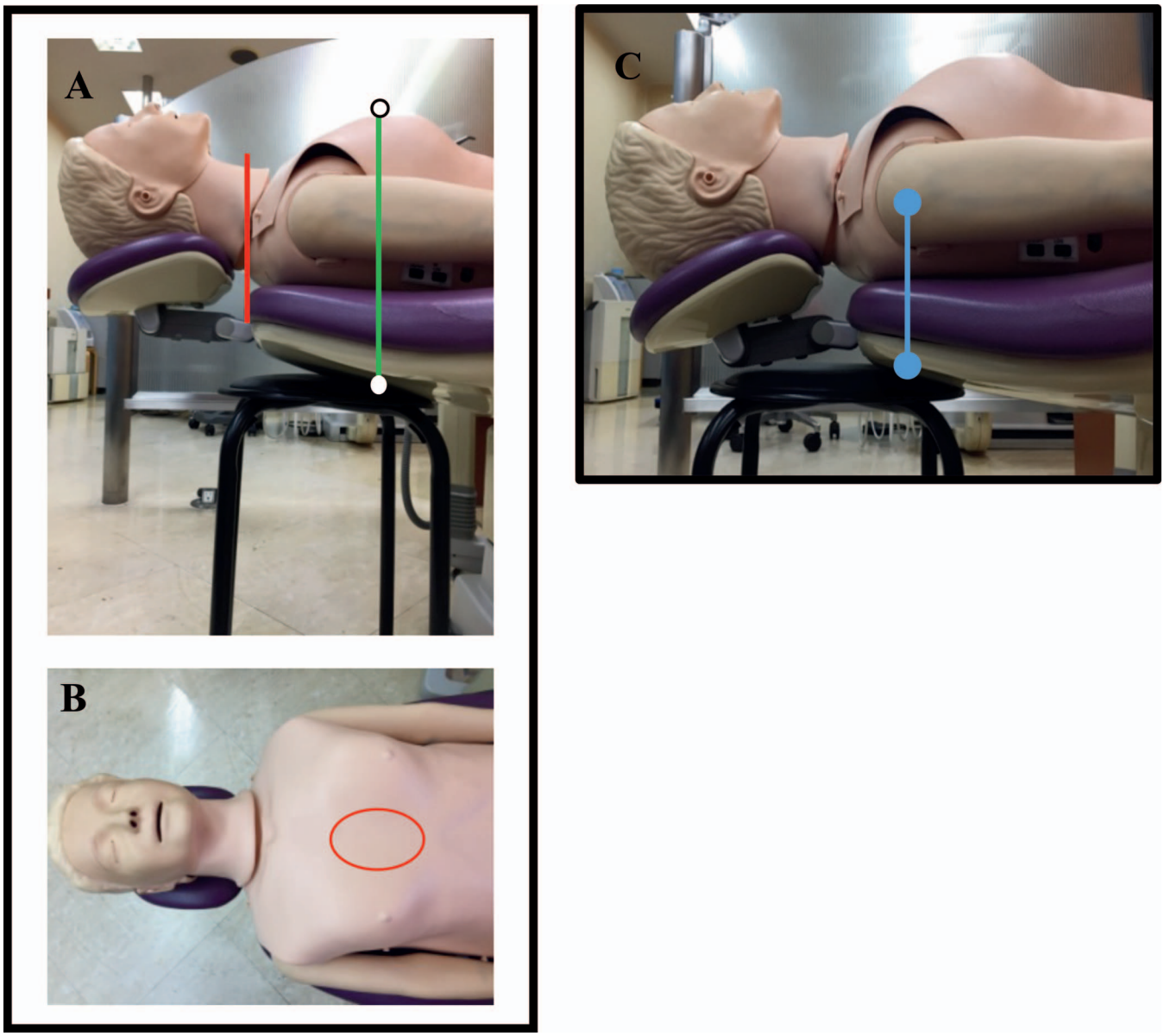

Figure 1. Manikin setup and positioning of the stabilizing stool. Upper end of the manikin torso was aligned with the top edge of the backrest (A; red line). The superior surface of the backrest under the lower half of the manikin sternum was positioned horizontally using a levelling instrument. The edge of the stool's seating surface was set to touch the backrest vertically under the area for manual chest compressions (A; green line). The center of the manikin's chest (B; red ellipse) was the hand position during chest compressions. The stool was set to touch the backrest vertically under the shoulders (C; blue line).

curved exterior during CPR using our method. This study showed that the stool placed under the patient's shoulder area substantially reduced the vertical displacement of the dental chair compared with the stool positioned under the area of MCC as evident by the significant difference in calculated reduction ratios. The difference in support efficiency between the 2 stool positions was attributed to the area of contact between the stool and the curved exterior of this particular chair design. Although the stool was positioned under the area of MCC, the area where the stool contacted the backrest was smaller and provided less support than when the stool was positioned under the shoulders. This study's data demonstrate that the use of a stool positioned under the shoulders is more effective for backrest stabilization during MCC allowing health care providers to perform effective CPR in a dental chair with a severely curved backrest exterior.

AHA and ERC current guidelines emphasize the importance of minimizing interruptions during MCC

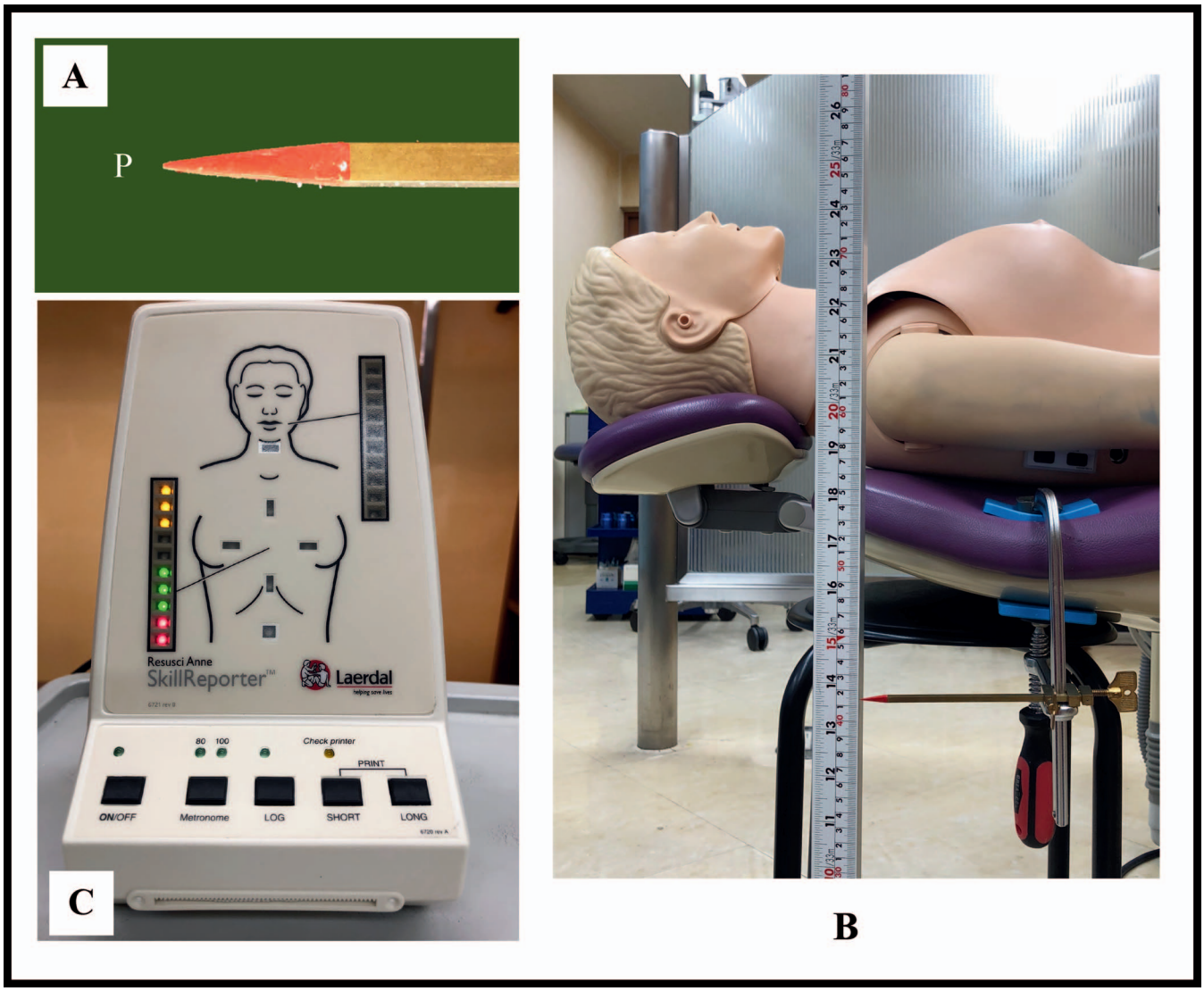

Figure 2. Measuring vertical displacement and chest compression depth. A metal indicator (point P; A) was made parallel to the floor with a leveling gauge and secured to the inferior surface of the dental chair directly under the area for manual chest compression (MCC) next to a fixed vertical-measurement instrument (B). The distance of point P relative to the inferior surface of the backrest remained fixed. Chest compression depth was assessed using the manikin's SkillReporter system (C) with green lights indicating chest compression depths of 5.1–6.0 cm and red lights for 3.8–5.0 cm.

Vertical Displacement Measurements and Calculated Reduction Ratios*

	Vertical displacement (mm)	*Reduction ratio (%)*	*P value*
No stool	16.5 (2.5)	–	
Stool under MCC	12.0 (1.5)	27% (20)	<.001
Stool under shoulders	8.5 (1.0)	48% (14)	

* Measurements of dental chair backrest vertical displacement during manual chest compression (MCC) and calculated reduction ratios. Results expressed as median (interquartile range).

while also pushing hard and fast. MCC should be started on a stable surface (ie, a dental chair) as soon as possible whenever cardiac arrest is suspected.[6,7] However, when CPR is performed on a patient in a dental chair, the backrest may not be supportive enough for effective resuscitation as a large vertical displacement of the backrest might negatively impact the efficacy of MCC.[8–11] In our previous study, a stabilizing stool placed just under the area of MCC significantly reduced backrest displacement during MCC in all 8 dental chairs evaluated.[2,4] However, the stool's supportive efficiency was found to vary between the different dental chair designs, likely due to the shape of the chair's exterior.

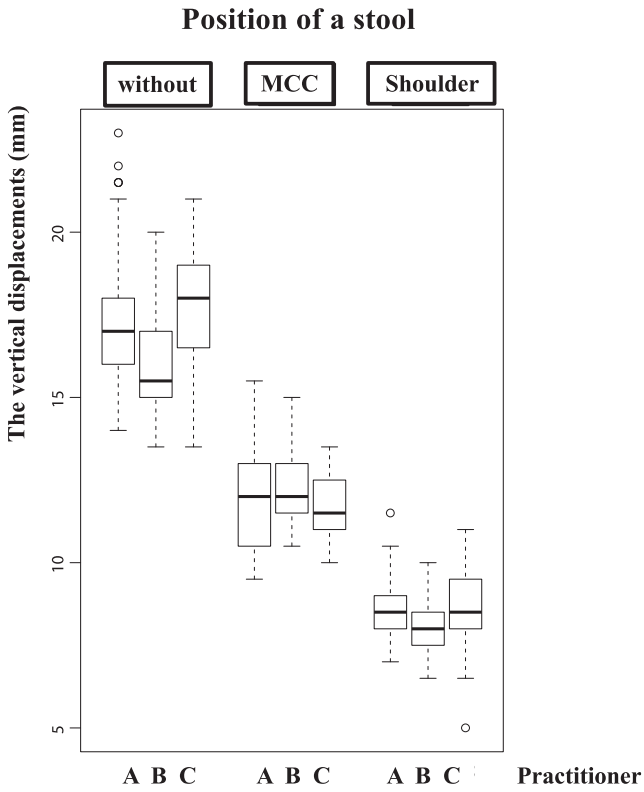

Figure 3. Vertical displacement measurements for each participant. Effect of the stabilizing stool on the backrest vertical displacement measurements during chest compressions. The thick lines represent median values, the boxes represent interquartile ranges, over and under lines represent date ranges, and circles represent outliers.

The backrest displacement seemed to be negatively impacted by lateral movement of the supporting stool, which moved slightly during every chest compression. Although lateral stool movements were not directly analyzed in this study, the stool was observed moving laterally on the video data several times. In a dental chair with a severely curved backrest exterior and a stabilizing stool set just under MCC, the contacted area between the stool and the backrest would likely be small, and the forces during compressions may be applied not only vertically but also horizontally causing lateral movement of the stool.

Many commercial dental chairs have curved ergonomic backrest designs, which tend to gradually become flatter moving superiorly up to the patient's shoulder area. The chair exterior below the area of MCC often has a more pronounced curvature, which negatively impacts the contact point of the stool and reduces stabilization. The chair exterior has a flatter shape more superiorly, which provides a larger wider contact area for the stabilizing stool when positioned under the shoulders. In this situation, the stool significantly reduced vertical displacement during MCC, producing a larger calculated reduction ratio when positioned under the shoulders (48%) compared with under the area of MCC (27%). Additionally, the stool can also support the dental chair headrest when positioned more superiorly, which may also be useful in suppressing lateral movements of the stool during compressions.

This study had several limitations. First, this study included only 1 type of chair, and although this is a common model, there are many types of dental chairs used throughout the world. Second, this study was performed with the use of a manikin model, so careful extrapolation of the results to human patients is indicated. Third, this study did not consider the effect of the dental chair cushioning nor the use of a firm backboard during MCC.[12,13] Next, the stool was set in 2 particular positions: under the area of MCC and under the shoulders. Additional studies should be conducted to evaluate other positions for the stabilizing stool to determine maximum effectiveness. Finally, the usefulness of other types of stabilizers remains to be verified. However, no studies to date have demonstrated a significant reduction in vertical displacement by using a stool for support with a dental chair that has a curved exterior shell. Positioning a stool to support the dental chair backrest is a very easy and effective method for increasing the efficacy of MCC and should be utilized when performing CPR on a patient in a dental chair. If it is difficult to move the patient to the floor quickly and safely, this technique should ideally be combined with the insertion of a rigid backboard between the patient's back and the cushion of the dental chair.

CONCLUSION

In dental chairs with a severely curved exterior shape, the use of a stabilizing stool positioned under the shoulder area significantly reduced backrest vertical displacement compared with a stool positioned under the area of MCC. This technique is convenient and useful for providing more effective chest compressions if CPR is emergently required for a patient in a dental chair with a curved exterior shell.

ACKNOWLEDGMENTS

All procedures were performed in studies performing on a manikin model. This article does not contain any studies with human participants or animals performed by any of the authors. For this type of study, formal consent is not required. We consulted the institutional review board at Kyushu University, which confirmed

that no formal written waiver for ethics approval was required, because of the design of the study. In addition, there was no written consent needed from 3 health care providers. Data sets from the current study are available from the corresponding author upon reasonable request. All authors have no conflict of interest.

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A Survey of Dentist Anesthesiologists on Preoperative Intramuscular Sedation

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Objective: The induction of general anesthesia for children and patients with special needs frequently requires preinduction sedation, especially when anxiety and agitation lead to violent or combative behavior. In these situations, preoperative intramuscular (IM) sedation may facilitate patient transfer, intravenous cannulation, and/or mask induction. This survey aimed to capture data regarding the current preoperative IM sedation practices of dentist anesthesiologists.

Methods: An electronic survey was distributed in 2020 to all members of the American Society of Dentist Anesthesiologists regarding the administration of preoperative IM sedation. It included questions about the demographics of respondents and their patients who require IM sedation, the most common drug regimens used, decision-making criteria regarding ketamine dosing, the intended level of sedation, sequence of anesthetic management following IM sedation, and observed outcomes.

Results: A total of 193 responses (43%) were received; of those, 162 reported using preoperative IM sedation. Ketamine was included in 98.7% of reported IM drug regimens. The most common IM sedation regimen was combined ketamine and midazolam (median 2.5 mg/kg and 0.1 mg/kg, respectively). Of the respondents who use preoperative IM sedation, 87% reported using the same drug regimen in at least 80% of cases.

Conclusion: The most frequently reported drug regimen used by dentist anesthesiologists in North America for preoperative IM sedation was a combination of ketamine and midazolam.

Key Words: Intramuscular premedication; Ketamine; Dexmedetomidine; Midazolam; Preoperative sedation; Autism spectrum disorder; Special needs; Dental anesthesia.

General anesthesia induction for children and patients with special needs can be very challenging, as patient anxiety and agitation can cause preoperative disturbances and disrupt clinic schedules. In extreme circumstances, violent or combative behavior poses a physical risk to the patient, their caregivers, and health care personnel. In these situations, preoperative intramuscular (IM) sedation is often used to facilitate safe transfer to the operating room (OR) and intravenous (IV) cannulation, with the primary goal being behavior modification.

There are neither clear guidelines for preoperative IM sedation nor data about the practice patterns of dentist anesthesiologists who use this technique. Specifically, it is not known what drug regimens are typically used, how frequently preoperative sedatives are administered by the IM route, what factors influence clinical decisions regarding the use of preoperative IM sedation, or what the perceived success of preoperative IM sedation is. We conducted a survey of dentist anesthesiologists in North America to characterize their current use of preoperative IM sedation in clinical practice.

METHODS AND MATERIALS

We conducted an institutional review board–approved survey of dentist anesthesiologists regarding their current use of preoperative IM sedation prior to the induction of general anesthesia. The survey was administered electronically through Qualtrics in April

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2020, and email invitations were sent to all members (447) of the American Society of Dentist Anesthesiologists (ASDA). Follow-up emails were sent 2 weeks later. Responses were accepted from April 24, 2020, through May 26, 2020. Participation was voluntary with no offered incentive for completion. The survey included 13 items assessing respondent and patient demographics, frequency of preoperative IM sedation use, practice location, drugs and dosages used, the intended level of sedation using the Richmond Agitation and Sedation Scale (RASS), success at achieving the intended level of sedation, use of anticholinergics, factors influencing ketamine dosing, and occurrence of select adverse events (Appendix 1).

Statistical Analysis

All surveys were evaluated for completeness and quality. Surveys were excluded if respondents failed to identify as a dentist anesthesiologist or failed to answer any questions beyond demographics. Any inappropriate responses to individual questions were also excluded from analysis for that question only (e.g., providing non–weight-based dosages for preoperative IM sedation drugs or listing percentages not summing to 100%). When respondents provided a dose range rather than a single dose, the calculated midpoint was used for analysis.

Where noted in the tables, a weighting factor was applied to specific responses, and a weighted average was calculated to better characterize the data. For example, survey question 13 allowed respondents to select 1 of the following options regarding the number of adverse events observed over the last year after preoperative IM sedation: 0, 1 to 2, 3 to 5, or >5. A weighting factor of 0, 1.5, 4, and 8 was applied to each choice, respectively. This weighting factor was multiplied by the number of respondents who selected each option, and the total results were averaged.

Descriptive data analysis was performed using Microsoft Excel version 16.35 (Microsoft). Distribution of the reported ketamine dosing regimen was examined for normality using the Shapiro-Wilk test and found to be not normally distributed. Therefore, Wilcoxon rank-sum tests were performed to examine the differences in reported ketamine dosing by several practice-related variables. Analyses were performed using SAS version 9.4. Where applicable, $P < .05$ was considered statistically significant.

RESULTS

Overall, 447 surveys were distributed to the ASDA membership, 193 responses were received (43% overall response rate), and a total of 180 responses were included for analysis. Of the 13 excluded surveys, 6 were due to failed identification as a dentist anesthesiologist and 7 were due to respondents not answering any questions regarding IM drug regimens. A high percentage of responses to question 6 were deemed inappropriate; therefore, all responses to question 6 were excluded from the analysis. Most respondents (91%) reported using preoperative IM sedation at least once annually, and of those, 42% reported more than 100 cases involving preoperative IM sedation (Table 1).

Of the 151 respondents who provided their most common drug regimen for preoperative IM sedation, 149 (98%) use a ketamine-based drug regimen (Tables 2 and 3). The most frequently reported drug regimen was ketamine with midazolam (52%; median 2.5 mg/kg and 0.1 mg/kg, respectively), followed by ketamine alone (32%; median 3 mg/kg). Less commonly reported adjunctive IM sedatives were dexmedetomidine, fentanyl, meperidine, and clonidine (reported in 16, 4, 3, and 1 IM regimens, respectively).

Table 4 displays the respondents' clinical practice patterns regarding preoperative IM sedation. A large majority of respondents (87%) indicated that they administer the same drug regimen in ≥80% of cases requiring preoperative IM sedation. Most respondents (96%) target a RASS score of –3, –4, or –5 after administering preoperative IM sedation. Similarly, 96% of respondents report achieving their anticipated level of sedation in >80% of cases. A small majority of respondents (51%) routinely administer anticholinergics with IM ketamine. When an anticholinergic is administered, IV glycopyrrolate is the most common drug and route of administration (24%). After administering preoperative IM sedation, most providers (74%) establish IV access next in their anesthetic management sequence.

Select side effects were reported to be infrequent among all providers (Table 5). The most common unwanted side effect was dysphoria, either immediately postinjection or on emergence from general anesthesia.

Providers also identified the importance of multiple factors when determining their dose of IM ketamine (Table 6). The highest scoring responses were "preinjection patient behavior/agitation" and "certainty of IM effect."

As seen in Table 7, further analysis was undertaken to understand whether there were any statistically significant differences in ketamine dosages when comparing selected subgroups of respondents. Anesthesiologists who typically start an IV after IM sedation reported a higher ketamine dose compared with those who typically start with an inhalational induction after IM sedation (median 3 vs 2 mg/kg; $P = .0002$). A

Table 1. Respondent and Patient Demographics*†

	Total respondents (N = 180)	*Responses by venue*		
		Hospital OR	*Hospital NORA/ASC/dental school*	*Office*
Use of preoperative IM sedation, n (%)	164 (91)	12 (7)	36 (20)	116 (64)
Years in practice,‡ n (%)				
0-5	51 (28)	5 (3)	11 (6)	35 (19)
6-10	44 (24)	2 (1)	7 (4)	31 (17)
11-20	32 (18)	2 (1)	6 (3)	21 (12)
21-30	19 (11)	0 (0)	8 (4)	11 (6)
>30	27 (15)	3 (2)	4 (2)	16 (9)
Teaches residents or fellows, n (%)	67 (37)	12 (7)	22 (12)	33 (18)
Annual number of cases using preoperative IM sedation,§ n (%)				
<6	24 (15)	2 (1)	7 (4)	15 (9)
6-25	35 (22)	4 (2)	8 (5)	23 (14)
26-50	15 (9)	1 (1)	8 (5)	6 (4)
51-100	20 (12)	1 (1)	5 (3)	14 (9)
101-500	45 (28)	4 (2)	7 (4)	34 (21)
>500	23 (14)	0 (0)	1 (1)	22 (14)
Percentage of annual patients treated with preoperative IM sedation‡§				
Typical children ages 2-12 y	45	31	29	51
Special needs children ages 2-12 y	20	24	17	21
Specials needs ages 13 y and older	35	45	54	27

* Abbreviations: ASC, ambulatory surgical center; NORA, non–operating room anesthesia; OR, operating room.

† Descriptive data provided by respondents to questions regarding demographics, with columns segregating data based on the most common venue in which respondents administer preoperative IM sedation. In some cases, the total numbers may be different than the sum of each respective column; this is due to respondents leaving selected questions unanswered.

‡ Inaccurate sum totals reflect missing respondent data, and percentages may not total 100 due to rounding.

§ Denotes n = 162.

significantly higher median dose of ketamine (3 vs 2 mg/kg; $P = .007$) was reported by anesthesiologists who expected a deeper level of sedation (RASS 4 or 5 vs RASS 1, 2, or 3). No other selected comparisons reached the threshold for statistical significance.

DISCUSSION

Most dentist anesthesiologists provide general anesthesia in the dental office setting. When treating children or patients with special needs, the two most common routes of general anesthesia induction are inhalation or IM. Some dentist anesthesiologists travel with portable anesthesia machines. These providers are likely to induce general anesthesia by the inhalational route. However, when the patient is physically combative, or when an anesthesia machine is not available, providers are likely to induce general anesthesia by the IM route.

Preoperative IM sedation typically occurs in nontreatment areas of private offices or in the preoperative holding area of hospitals or ambulatory surgical centers prior to any formal patient monitoring. In rare instances, due to emotional distress, behavioral defiance, or physical limitations, preoperative IM sedation may even be administered in a vehicle parked at the hospital or treatment facility. It is critical that the sedative regimen achieves an adequate level of sedation predictably, rapidly, and safely. Once adequate sedation has been achieved, the patient can be separated from caregivers and transported to the desired location. The order of the subsequent sequence of events may vary depending on the preferences of the anesthesia providers and the available resources or the level of sedation achieved. In general, these events include transfer to the OR/dental operatory, placement of anesthesia monitors, IV cannulation, and induction (either IV or inhalation) of general anesthesia.

Although recommendations can be found in various anesthesia sources regarding ketamine-based drug regimens for preoperative IM sedation, there are no clear

Table 2. Most Common Preoperative IM Sedation Drug Regimens*

IM drug regimen	*Value, n (%), N = 151*
Ketamine alone	48 (32)
Ketamine and midazolam	79 (52)
Ketamine and dexmedetomidine	3 (2)
Ketamine, midazolam, and dexmedetomidine	11 (7)
Ketamine plus other drugs	8 (5)
Non–ketamine-based drug regimen	2 (1)

* IM, intramuscular.

Table 3. Most Common Preoperative IM Sedation Drug Dosages by Venue*

IM drug dosing	*Median (IQR)*	*By venue, median*		
		Hospital OR	*Hospital NORA/ASC/dental school*	*Office*
Ketamine alone, mg/kg	3 (2-3)	3	2.5	3
Ketamine and midazolam				
Ketamine, mg/kg	2.5 (2-3)	5	2.5	2.5
Midazolam, mg/kg	0.1 (0.07-0.1)	0.05	0.1	0.1
Ketamine and dexmedetomidine				
Ketamine, mg/kg	3 (n/a)	3	n/a	2.75
Dexmedetomidine, mcg/kg	0.5 (n/a)	1	n/a	0.4
Ketamine, midazolam, and dexmedetomidine				
Ketamine, mg/kg	2.3 (2-3)	3.5	2	2
Midazolam, mg/kg	0.1 (0.09-0.1)	0.3	0.1	0.1
Dexmedetomidine, mcg/kg	1 (0.4-1.6)	2	0.3	1

* ASC, ambulatory surgical center; IM, intramuscular; IQR, interquartile range; n/a, not applicable; NORA, non–operating room anesthesia; OR, operating room.

guidelines about the most effective drugs, drug combinations, or dosages. Furthermore, there are minimal data regarding dentist anesthesiologists' current practice habits regarding IM sedation and the safety of these techniques. The questions in this survey were designed to characterize current practices of individual dentist anesthesiologists including demographic data about providers, practice location, frequency of preoperative IM sedation, drug regimens (both drugs and dosages), next steps after IM sedation, the intended RASS level of

Table 4. Practice Patterns*†

	Total (N = 156)	*By venue*		
		Hospital OR	*Hospital NORA/ASC/dental school*	*Office*
Frequency of using most common IM drug regimen, n (%)				
100%	40 (26)	6 (4)	8 (5)	26 (17)
90-99%	74 (47)	1 (1)	13 (8)	59 (38)
80-89%	21 (13)	3 (2)	3 (2)	15 (10)
60-79%	16 (10)	2 (1)	7 (4)	7 (4)
<60%	5 (3)	0 (0)	2 (1)	3 (2)
Routine anticholinergic administration with ketamine, n (%)				
N/A	1 (1)	0 (0)	0 (0)	1 (1)
No	75 (48)	7 (4)	11 (7)	57 (37)
IV glycopyrrolate	37 (24)	3 (2)	10 (6)	24 (15)
IV atropine	15 (10)	0 (0)	4 (3)	10 (6)
IM glycopyrrolate	24 (15)	2 (1)	8 (5)	14 (9)
IM atropine	4 (3)	0 (0)	0 (0)	4 (3)
Typical intervention after IM sedation, n (%)				
Start IV	116 (74)	7 (4)	31 (20)	77 (49)
Mask induction	33 (21)	3 (2)	1 (1)	29 (19)
Other	7 (4)	2 (1)	1 (1)	4 (3)
Expected RASS level of sedation, n (%)				
RASS −5	20 (13)	3 (2)	0 (0)	17 (11)
RASS −4	92 (59)	5 (3)	21 (13)	66 (42)
RASS −3	37 (24)	4 (3)	10 (6)	23 (15)
RASS −2	5 (3)	0 (0)	1 (1)	4 (3)
RASS −1	2 (1)	0 (0)	1 (1)	1 (1)
Frequency of attaining expected RASS level of sedation, n (%)				
100%	9 (6)	1 (1)	1 (1)	7 (4)
90-99%	101 (65)	9 (6)	18 (12)	74 (47)
80-89%	39 (25)	2 (1)	11 (7)	26 (17)
60-79%	6 (4)	0 (0)	3 (2)	3 (2)
<60%	1 (1)	0 (0)	0 (0)	1 (1)

* Abbreviations: ASC, ambulatory surgery center; IM, intramuscular; IV, intravenous; NORA, non–operating room anesthesia; OR, operating room; RASS, Richmond Agitation Sedation Scale.

† Inaccurate sum totals reflect missing respondent data, and percentages may not total 100 due to rounding.

Table 5. Unwanted Side Effects and Adverse Events*

Event	*Number†*
Dysphoria (emergence)	2.05
Dysphoria (postinjection)	1.90
Vomiting	0.93
Laryngospasm	0.63
Desaturation (SpO_2 <90%)	0.58

* The average reported number of events that occurred in the previous year for each provider.

† Survey question 13 ("In last year, in how many patients did you observe the following adverse events after using preoperative IM sedation?") allowed respondents to select 0, 1 to 2, 3 to 5, and >5 to which a corresponding weighting factor of 0, 1.5, 4, or 8 was applied.

Table 6. Ketamine Dose Decision*†

Factor	*Importance‡*
Certainty of IM effect	3.1
Preinjection patient behavior/agitation	2.9
Use the lowest dose possible	2.5
Rate of onset of sedation	2.4
Duration of recovery	2.1
Patient appearance at parental separation	2.1
Duration of procedure	1.9
Incidence of psychomimetic reactions	1.7

* Abbreviation: IM, intramuscular.

† List of the average relative importance of factors that may affect ketamine dosing.

‡ Survey question 12 ("In determining your dose of IM ketamine for preoperative sedation, how important are the following considerations?") allowed responses ranging from not, slightly, moderately, very, and extremely important, to which a corresponding weighting factor of 0, 1, 2, 3, or 4 was applied.

sedation, the success of achieving this level of sedation, use of anticholinergics, factors that influence ketamine dosages, and adverse events. The highest reported drug regimen was a combination of ketamine and midazolam (median 2.5 mg/kg and 0.1 mg/kg, respectively), with the second most being ketamine alone (median 3.0 mg/kg). Dysphoria observed immediately after injection or upon emergence were the most reported side effects, with 67% of respondents reporting at least 1 case in the previous year.

Ketamine is widely used for IM sedation because it rapidly and predictably produces immobility, amnesia, analgesia, and a classic "dissociative" state in which airway reflexes and respiratory drive are largely preserved.[1] The US Food and Drug Administration (FDA) package insert for ketamine alternately references IM doses of 9 to 13 mg/kg and 6.5 to 13 mg/kg to produce 12 to 25 minutes of surgical anesthesia but makes no statement about the use of ketamine specifically for preoperative IM sedation.[2] The Emergency Medicine (EM) guidelines for procedural sedation recommend an IM ketamine dose of 4 to 5 mg/kg noting, "there is no apparent benefit . . . to using 3 mg/kg rather than 4 to 5 mg/kg IM, except perhaps a slightly faster recovery with the lower dose."[3] Emergency procedures (eg, fracture reduction) requiring IM sedation are often painful yet brief and rely in part on the analgesia produced by ketamine. In addition, these EM guidelines recommend against the routine use of a benzodiazepine or anticholinergic due to a lack of evidence demonstrating improved patient outcomes in that setting. Preoperative IM sedation is distinct from surgical anesthesia (as noted in the FDA label) or procedural sedation (as addressed by the EM guidelines) in that only behavior modification is required to facilitate separation from caregivers, transfer to the OR, establishment of IV access, and/or induction of general anesthesia. Unfortunately, the anesthesia literature is relatively silent on the issue of ideal drug regimens for preoperative IM sedation.

A comparison of some of the most popular anesthesia textbooks provides a wide range of recommendations regarding preoperative IM sedation. Jaffe recommends ketamine 2 mg/kg with midazolam 0.2 mg/kg and glycopyrrolate 0.1 mg/kg.[4] *Morgan & Mikhail's Clinical Anesthesiology* suggests midazolam 0.1 to 0.15 or ketamine 2 to 3 mg/kg with atropine 0.02 mg/kg.[5] *Miller's Anesthesia* suggests ketamine 4 to 5 mg/kg IM for reduction of anxiety and 5 to 10 mg/kg to induce general anesthesia.[6] Furthermore, this text also suggests IM coadministration of a benzodiazepine to reduce hallucinations and an anticholinergic to reduce sialorrhea but specifies neither specific agents nor dosages. *Basics of Anesthesia* recommends ketamine 5 mg/kg and notes that IM atropine or glycopyrrolate can be used (but does not specify an anticholinergic dose).[7]

Cote's *A Practice of Anesthesia for Infants and Children* offers a more detailed discussion of ketamine and preoperative IM sedation, beginning with the observation that ketamine 2 mg/kg will calm most children enough to accept a mask without prolonging discharge times, while the addition of midazolam 0.1 to 0.2 mg/kg may prolong recovery and discharge times after very short procedures.[8] Cote also notes that larger doses of ketamine (eg, 4-5 mg/kg) may be used for a more rapid onset of sedation or when maintenance of blood pressure is important, such as in the treatment of patients with congenital heart disease, and that ketamine 10 mg/kg will produce deep sedation for a period of 12 to 25 minutes. Cote recommends routine administration of an anticholinergic to reduce ketamine-induced sialorrhea but clarifies that IV administration is usually

Table 7. Ketamine Dose Comparison*†

Comparison	*Ketamine dose, median (IQR)*	*P value*
Inhalational induction	2 (2, 2.5)	.0002‡
IV induction	3 (2, 3)	
Hospital OR	3 (2.5, 3)	.08
Office	2.5 (2, 3)	
Ketamine alone	2.5 (2, 3)	.32
Ketamine with another sedative	3 (2, 3)	
High-use providers (>100 IM cases/y)	2.5 (2, 3)	.63
Low-use providers (<26 IM cases/y)	3 (2, 3)	
In practice 0-5 years	2.5 (2, 3)	.89
In practice >20 years	3 (2, 3)	
Preoperative patient behavior very/extremely important	2.5 (2, 3)	.42
Preoperative patient behavior not/slightly/moderately important	3 (2, 3)	
Certainty of IM effect very/extremely important	2.5 (2, 3)	.33
Certainty of IM effect not/slightly/moderately Important	3 (2, 3)	
Expected RASS −1/−2/−3	2 (2, 3)	.007‡
Expected RASS −4/−5	3 (2.2, 3)	
50% or more of patients special needs 13 y and older	2.5 (2, 3)	.05
<50% of patients special needs 13 y and older	2.9 (2, 3)	

* Abbreviations: IQR, interquartile range; IM, intramuscular; IV, intravenous; OR, operating room; RASS, Richmond Agitation Sedation Scale.

† For the purposes of these comparisons, no adjustments were made whether ketamine was administered alone or with other sedatives.

‡ Denotes $P < .05$.

sufficient once IV access has been established as opposed to IM coadministration with ketamine. In addition, Cote also notes that glycopyrrolate is twice as effective as an antisialagogue when compared with atropine. In short, there is little agreement in the major anesthesia texts regarding the best approach to preoperative IM sedation.

In this survey, the single highest reported dosage of IM ketamine was 5 mg/kg (ketamine with midazolam 0.07 mg/kg). Of the 149 ketamine dosages reported (with or without adjunctive sedatives), 82% ranged from 2 to 3.5 mg/kg (8% were ≥4 mg/kg, and 10% were <2 mg/kg). In addition to using lower ketamine dosages than found in the FDA package insert or in the EM guidelines for procedural sedation, respondents frequently (67%) rely on adjunctive sedatives, such as midazolam or dexmedetomidine, for preoperative IM sedation. Interestingly, the reported ketamine dosages were minimally altered whether used alone or with adjunctive sedatives. In addition, despite published evidence showing that the combination of IM ketamine with midazolam can prolong recovery after very short procedures,[9] data from this survey suggest prolonged recovery time does not appear to be a primary concern for most dentist anesthesiologists. This may be because most dental procedures requiring general anesthesia are at least 45 minutes in length. Individual dentist anesthesiologists are generally consistent with their preoperative IM sedation drug regimens. Although reported drug regimens varied widely, most providers also reported a high success rate with their chosen drug regimen, as determined by the percentage of cases in which providers reported achieving their desired RASS level of sedation.

This survey had several limitations. As a survey, respondents' answers are subject to several biases. These include recency bias (the tendency to give higher importance to recent events), recall bias (incomplete memories), response bias (incorrect or untruthful responses produced by survey design, perceived "right" answers, or other factors), reporting bias (selective event reporting), and participation bias (systematic differences between those who responded to the survey and those who did not).

The survey does not fully characterize the resources of each anesthesia provider. For example, some office-based providers may not have access to inhalational anesthetics, and this limitation may affect their preoperative IM sedation drug regimen. In addition, this survey did not specifically address why providers use their selected regimens or why providers may alter their selected drug regimens. For example, a provider may administer one drug regimen to a healthy child and an alternative drug regimen to a combative, nonverbal adult male with autism spectrum disorder. This survey was not designed to address causality between adverse events and preoperative IM drug regimens. There is also the possibility that unclear wording of questions may have led to unintentionally inappropriate responses.

CONCLUSION

In summary, this survey captures dentist anesthesiologists' current practice patterns regarding preoperative IM sedation. We report that ketamine-based drug regimens are the primary choice for preoperative IM sedation and that ketamine is frequently coadministered with midazolam or other sedatives. Prospective research is needed to identify the differences in effects produced by various preoperative IM sedation drug regimens in different patient populations.

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Anesthetic Management of a Patient With Catecholaminergic Polymorphic Ventricular Tachycardia

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Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a rare inherited arrhythmogenic disorder induced by adrenergic stress. Electrophysiologically, it is characterized by emotional stress- or exercise-induced bidirectional ventricular tachycardia that may result in cardiac arrest. Minimizing perioperative stress is critical as it can reduce fatal arrhythmias in patients with CPVT. Dexmedetomidine (DEX), a centrally acting sympatholytic anesthetic agent, was used in the successful intravenous (IV) moderate sedation of a 27-year-old female patient with CPVT, a history of cardiac events, and significant dental fear and anxiety scheduled to undergo mandibular left third molar extraction. Oral surgery was successfully performed under DEX-based IV sedation to reduce stress, and no arrhythmias were observed. IV sedation with DEX provided a sympatholytic effect with respiratory and cardiovascular stability in this patient with CPVT who underwent oral surgery.

Key Words: Catecholaminergic polymorphic ventricular tachycardia; Sudden cardiac death; Intravenous sedation; Dexmedetomidine.

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a rare inheritable arrhythmogenic disorder characterized by physical or emotional stress-induced polymorphic ventricular tachyarrhythmias or bidirectional ventricular tachycardia without any detectable morphological cardiac abnormalities.[1–3] CPVT is a common cause of sudden cardiac death in young otherwise healthy patients, with cardiac events being induced by sympathetic activation and catecholamine release during physical and emotional stress.[3] Syncope is the most frequent symptom and often leads to a misdiagnosis of epilepsy.[2] It is frequently difficult to establish a timely and accurate diagnosis due to normal cardiac imaging, unremarkable baseline electrocardiograms (ECGs), and commonly misattributed syncopal episodes. Early and prompt recognition of CPVT is critical due to its high mortality rate (up to 50%) in severely affected untreated patients by the age of 20 years.[2] Mutations in the *RYR2* gene encoding cardiac ryanodine receptor calcium ion release channels are the leading causes of CPVT.[4,5]

Regarding the anesthetic management of patients with CPVT, active measures are needed to reduce stress and anxiety throughout the perioperative period. Because invasive dental procedures, including oral surgery, can induce emotional stress, these patients require sedation or general anesthesia. Dexmedetomidine (DEX) is a highly selective centrally acting α2-adrenoceptor agonist that has 8 times greater specificity for α2 receptors than clonidine.[6] DEX exerts antihypertensive, analgesic, and sedative effects by inhibiting endogenous catecholamine release at adrenoreceptors located on the substantia gelatinosa of the spinal cord and the locus coeruleus of the brain.[6,7] DEX is often administered in surgical procedures requiring intravenous (IV) sedation,[8,9] as well as in the intensive care unit and is thought to have less respiratory depression than other sedatives.[10,11] However, airway obstruction and apnea with DEX has been noted in several studies.[12,13] It also reduces catecholamine secretion, thereby reducing stress and modestly decreasing heart rate (HR) and blood pressure (BP).[6] Therefore, the centrally acting

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sympatholytic effects of DEX could be useful in patients with adrenergic-dependent syndromes, including CPVT. We describe the anesthetic management protocol for DEX-based IV sedation of a patient with CPVT, dental anxiety, and a history of cardiac events. Informed consent to publish case details was obtained from the patient.

CASE PRESENTATION

The patient was a 27-year-old woman (height, 152 cm; weight, 45 kg; body mass index, 19.5 kg/m^2) with a significant cardiac history. At 7 and 8 years of age, she experienced exercise-induced syncope. Because her resting ECG excluded long QT and Brugada syndrome and there was no structural heart disease evident per an echocardiogram, CPVT was suspected. Subsequent genetic testing identified a de novo RYR2 mutation that confirmed the CPVT diagnosis, and oral β-blocker administration was started immediately. The cardiologist recommended limiting vigorous physical activity, avoiding dehydration, and reducing anxiety-provoking situations. However, at 22 years of age she experienced emotional stress-induced syncope and regained consciousness while being transported in the ambulance. She had another episode of emotional stress-induced syncope at age 25, and the ECG obtained by paramedics on the scene showed ventricular tachycardia. She was transported to the local hospital where her rhythm was stabilized with IV β-blockers, and she was discharged on the following day.

The patient was scheduled to undergo mandibular left third molar extraction at our dental hospital; however, she expressed significant dental fear and anxiety. Considering her medical history and dental phobia, performing the surgical procedure under local anesthesia posed significant risk for cardiac events, including fatal arrhythmia. After discussion with the treating oral surgeon, the decision was made to treat her using IV moderate sedation (as assessed using the Observer's Assessment of Alertness/Sedation (OAA/S) scale for a target score of 3) to avoid endogenous catecholamine surges secondary to fear/anxiety or inadequate anesthesia.

The preoperative evaluation revealed a BP and HR of 107/47 mm Hg and 57 bpm, respectively. Her percutaneous oxygen saturation (SpO_2) was 97% on room air. No abnormalities were detected on routine preoperative ECG and blood tests, which consisted of a complete blood cell count, serum chemistry panel, and coagulation profile. Examination revealed a Mallampati class I airway. She reported taking nadolol 60 mg and flecainide 150 mg daily. She denied any family history of sudden cardiac or neonatal death and did not have an implantable cardioverter defibrillator (ICD).

On the day of the surgery, the patient presented to the dental hospital appropriately NPO (6 hours fasting; 2 hours no clear fluids) and took her usual morning dose of nadolol and flecainide. To prevent venipuncture stress-induced arrhythmia, a lidocaine patch (Penles Tape 18 mg, Nitto Denko Corporation) was applied to the IV site 30 minutes before she entered the operating room appearing anxious. American Society of Anesthesiologists monitors were placed, consisting of a pulse oximeter, 3-lead ECG, and a noninvasive BP cuff. Her initial vital signs were as follows: BP 105/61 mm Hg; HR 55 bpm; and SpO_2 98% on room air.

Oxygen 3 L/min was administered via nasal cannula. IV access was secured using a 22-gauge catheter placed in her left hand, and midazolam 2 mg was subsequently administered followed by DEX 6 mcg/kg/h continuous infusion. Her OAA/S score was 4 after 5 minutes with a BP, HR, and SpO_2 of 131/69 mm Hg, 47 bpm, and 100%, respectively. After 10 minutes, her OAA/S score decreased to 3 with a BP, HR, and SpO_2 of 131/68 mm Hg, 46 bpm, and 100%, respectively. The DEX infusion was then reduced to 0.4 mcg/kg/h with her respiratory status being stable, and the oral retractor was placed. Fifteen minutes following the start of sedation, additional midazolam 0.5 mg was administered followed by a left inferior alveolar nerve block using 2 mL of 0.75% ropivacaine (15 mg). An additional 3.6 mL of 3% mepivacaine (108 mg) was administered into the left posterior mandibular buccal gingiva.

The surgical procedure began 25 minutes following sedation initiation with her BP, HR, and SpO_2 being 117/64 mm Hg, 53 bpm, and 100%, respectively. Additional midazolam 0.5 mg was administered 35 minutes after initiating sedation. The patient did not complain of pain during the extraction as her OAA/S score remained at 3. During the operation, spontaneous respirations were maintained, and her mean arterial pressure ranged from 76 to 85 mm Hg, HR ranged from 49 to 56 bpm, and SpO_2 ranged from 99% to 100%. The DEX 0.4 mcg/kg/h infusion was discontinued upon surgery completion, and acetaminophen 1000 mg was also administered intravenously for postoperative analgesia. Total doses were midazolam 3 mg and DEX 56 mcg. Surgery time and sedation duration were 25 and 50 minutes, respectively. The patient remained calm until discharge ~90 minutes after completing surgery. She was fully awake and ambulatory at discharge and had no complications in the immediate postoperative period. The patient returned the next day for follow-up and expressed being satisfied with the sedation; moreover, she had no recall.

DISCUSSION

This case report demonstrated successful DEX-based IV sedation for dental extractions in a patient with CPVT. This protocol provided adequate intraoperative sedation for anxiety and stress reduction and prevented CPVT-induced fatal arrhythmias.

CPVT is a rare genetically inherited disorder characterized by syncope, arrhythmias, and potentially sudden death occurring during exercise or stress in children and young adults with morphologically normal hearts and normal baseline ECGs.[1–3] CPVT has an estimated prevalence of 1:10,000.[2] The disease typically presents as a history of syncope with physical exertion or acute emotional stress and has a reported median age of symptom onset of 10.8 years.[14] Syncope can lead to a misdiagnosis of epilepsy.[15] A family history of syncope or sudden death is positive in up to 30% of patients with CPVT.[16] Diagnosis of CPVT is based on the patient's history, exercise stress testing, and genetic testing. ECGs usually appear normal, and the CPVT diagnosis may be missed if an exercise stress test is not performed.[2]

In 2001, Priori et al[4] discovered that *RYR2* mutations underlie most CPVT cases, as this gene encodes proteins involved with the release of calcium from the sarcoplasmic reticulum and is rendered dysfunctional upon mutation. Fatal arrhythmias can be induced by the resulting imbalance in calcium ion concentration.[17,18] Bidirectional ventricular tachycardia may be triggered by delayed afterdepolarizations secondary to calcium overload.

Medical management of CPVT remains challenging. β-blockers reduce CPVT-induced ventricular arrhythmias and are indicated as a first-line treatment for symptom relief and prevention of sudden cardiac death. However, nonadherence and treatment failure usually occur.[19,20] Nadolol is often preferred due to its prolonged half-life.[2] Currently, the combined use of flecainide and β-blockers is considered superior to β-blocker monotherapy for reducing the risk of arrhythmic and symptomatic events, especially in patients with genetic mutations.[21] An ICD may be necessary for patients with recurrent life-threatening arrhythmias or episodes of cardiac arrest.[22] A recent multicenter study demonstrated the benefit of left cardiac sympathetic denervation in patients with CPVT.[23] There is currently no treatment that is completely effective or without risks. Moreover, cardiac and fatal or near-fatal events are often observed during long-term follow-up. In an analysis of 101 patients with CPVT with a mean follow-up of 7.9 years, Hayashi et al[3] reported cardiac events in 27 patients (27%), including 13 patients (13%) with fatal or near-fatal events. Because CPVT is epinephrine dependent, patients are instructed to abstain from competitive athletics and activities requiring physical exertion as well as to avoid emotional stress.

Anesthetic management, including IV sedation or general anesthesia, is required during oral surgery in patients with CPVT because stress- or anxiety-induced endogenous catecholamine release could cause ventricular arrhythmias or sudden cardiac death. However, few studies have reported IV sedation in patients with CPVT. We developed the anesthetic plan for this patient based on the following considerations: (1) avoiding endogenous catecholamine surges secondary to fear or inadequate levels of anesthesia and analgesia; (2) avoiding extrinsic catecholamines, especially β-adrenergic agonists; and (3) preparing to acutely manage ventricular tachycardia during the perioperative period. Anesthetics often used to manage patients with CPVT include sevoflurane, midazolam, propofol, fentanyl, and remifentanil.[24,25] Ketamine should be avoided because it stimulates sympathetic nervous system activity.

In order to avoid perioperative tachycardia, β-blocker therapy should be continued.[26] There have been reports of cardiac events following a missed β-blocker dose.[2,3] Moreover, the patient's usual β-blocker regimen may require supplementation, such as with short-acting IV β-blockers.[27] Esmolol, an ultra-short-acting cardioselective β1-adrenergic antagonist, attenuates hemodynamic responses to perioperative noxious stimuli.[28,29] However, its calculated dose should be reduced in the presence of underlying β-blockers. Therefore, IV β-blocker administration should be carefully considered. DEX, a novel α2-adrenergic agonist, exerts anxiolytic, sedative, analgesic, and sympatholytic effects with less respiratory depression than other sedatives.[6,7] DEX and esmolol have different pharmacokinetic profiles. Esmolol is a water-soluble agent that cannot pass through the blood-brain barrier and likely does not involve central β-receptors.[30] Contrastingly, DEX is a centrally acting sympatholytic agent that attenuates the stress response.[31] Central-acting α2-agonists attenuate HR, BP, and plasma catecholamine responses to sympathetic stimulation. Previous studies have shown that the α2-agonist clonidine is more effective in suppressing the sympathetic-mediated increase in plasma catecholamines than esmolol.[32,33] Therefore, we considered that the centrally acting sympatholytic effect of DEX could be more appropriate for adrenergic-dependent syndromes, including CPVT.

The level of consciousness during clinical DEX-based IV sedation is similar to that of natural sleep, wherein patients are easily arousable to stimulation. Therefore, sedating a patient with dental anxiety using DEX alone would likely be insufficient, possibly requiring another sedative. Moreover, it should be noted that IV DEX produces a biphasic BP response: an initial mean arterial

pressure increase and HR decrease, followed by a decrease in both. Potential DEX side effects include transient hypertension, hypotension, and bradycardia.[7] Most patients with CPVT routinely use β-blockers; therefore, careful HR monitoring is required during perioperative DEX administration. Because β-agonists (ie, epinephrine) may induce fatal arrhythmias in patients with CPVT, bradycardia should be treated with atropine. Propofol can attenuate the HR response to IV atropine,[34] so a combination of DEX and midazolam was used for IV sedation. A continuous low-dose DEX infusion was used because a high-dose DEX bolus can cause hypotension, bradycardia, and soft tissue airway obstruction.[35] Furthermore, anxiety-induced endogenous catecholamine release could have occurred before the DEX effect, so we consequently administered IV midazolam immediately after establishing IV access. Our patient's HR decreased from 55 to 46 bpm as an effect of the initial DEX dose. However, there was a gradual increase in the basal BP (105/61 mm Hg) until it reached its highest intraoperative value (131/68 mm Hg). We observed a biphasic hemodynamic response during DEX loading, and her BP returned to baseline levels. Because our patient remained hemodynamically stable, no atropine was given.

DEX is considered to cause less upper airway obstruction than propofol; however, a recent study by Lodenius et al[13] showed that at comparable levels of minimal to moderate sedation, DEX and propofol exhibited similar degrees of pharyngeal collapsibility and reductions in ventilatory drive. Spontaneous respirations and airway patency were maintained in our patient as the OAA/S score remained at 3. This suggests that in clinical situations requiring analgesia as well as sedation, the analgesic effect of DEX may allow lighter sedation than propofol and therefore less adverse ventilatory effects. In addition, sedatives like DEX and midazolam act synergistically, which allow dose reductions of each agent when used concomitantly.[36] In this case, the DEX and midazolam combination achieved an adequate sedative effect with stable respiratory and cardiovascular states.

Ensuring optimal perioperative analgesia is important in managing patients with CPVT. In patients with familial ventricular arrhythmias, dysrhythmias could be provoked by venipuncture pain.[37] A commercially available lidocaine patch is often used for topical anesthesia prior to venipuncture.[38] Because our patient did not report pain associated with vascular access, we believe that the lidocaine patch was useful. In addition, reducing preoperative anxiety by premedication (ie, an oral benzodiazepine) may help avoid fatal arrhythmias provoked by stress for patients with CPVT and dental anxiety.[24] DEX, which has an additional analgesic effect, could be effective for invasive oral surgery procedures in patients with CPVT.[8]

Epinephrine is used in local anesthetics to prevent systemic toxicity and promote hemostasis.[39] However, epinephrine-containing local anesthetics should be used carefully during dental procedures in patients with cardiac disease. A previous study found a 2- to 3-fold rise in plasma epinephrine values after 1.8 mL intraoral injections of 2% lidocaine with 1:100,000 epinephrine in healthy young patients.[40] Thus, when weighing the risks and benefits of epinephrine-containing local anesthetics for patients with CPVT, anesthesiologists should always consult with the patient's cardiologist. In this case, we used ropivacaine and mepivacaine plain for local anesthesia.

Moreover, postoperative pain may also lead to ventricular arrhythmias in patients with CPVT. Ropivacaine is a well-tolerated long-acting local anesthetic with a safer cardiotoxicity profile than bupivacaine,[41] and 0.75% ropivacaine has been used to achieve inferior alveolar nerve blocks of long duration to attenuate postoperative pain.[42] Our patient reported subjective lip and tongue numbness through discharge and well-controlled postoperative pain. Long-acting local anesthetics like ropivacaine can be effective options for controlling postoperative pain in patients with CPVT.

The most critical step in acute arrhythmia management in patients with CPVT could be recognizing the patient's concerns. When ventricular tachycardia occurs, front-line treatment is IV β-blockers.[20] Moreover, flecainide[14] and verapamil[43] may be effective while amiodarone is ineffective for patients with CPVT.[2] Epinephrine and other β-agonists can induce fatal arrhythmias. Administering a pure α-adrenergic agonist, like phenylephrine, may be a safe option for patients with CPVT. In the present case, we prepared phenylephrine, atropine, esmolol, and an external defibrillator in preparation for hemodynamic instability or an arrhythmia. However, defibrillation could also induce endogenous catecholamine release and further promote ventricular tachycardia. General anesthesia may further reduce stress, decreasing the risk of ventricular tachycardia, and could be an additional option.[20]

CONCLUSION

CPVT is characterized by catecholamine-induced fatal arrhythmias, which lead to syncope and sudden death. Because invasive surgical procedures can induce emotional stress in patients with CPVT, there is a need for anesthetic management. DEX-based IV sedation has a centrally acting sympatholytic effect, minimally impacts respiratory stability, and was successfully used in

combination with midazolam for oral surgery in a patient with CPVT. Use of DEX should be considered for the anesthetic management of patients with CPVT.

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General Anesthesia for a Dissociative Identity Disorder Patient With 20 Personalities: A Case Report

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Key Words: Dissociative identity disorder; Perioperative management; Delayed arousal; General anesthesia.

Dissociative identity disorder (DID) is a psychiatric condition characterized by multiple distinct personalities and repeated dissociative amnesia.[1] In this case, we performed general anesthesia on a DID patient with 20 distinct personalities that could emerge during periods of increased mental stress or anxiety. The patient was a 36-year-old man with a history of left cleft lip and palate undergoing a secondary alveolar bone graft from a tibial donor site. Several of his alternate personalities emerged during the perioperative period, including a 7-year-old boy who arrived the morning of surgery. However, by minimizing external stressors in the operating room and using a combination of propofol, sevoflurane, and remifentanil, we delivered general anesthesia safely without any emergence delirium or delayed awakening, and the surgery was successfully completed. Upon awakening, the patient was in his host personality and had no memory of entering the operating room. Postoperatively, the patient's personality switched several more times; however, there were no major issues, as we were able to identify the causes of his anxiety and stress, thereby minimizing the emergence of his alternative personalities.

Dissociative identity disorder (DID), formerly known as multiple personality disorder, is a psychiatric condition characterized by 2 or more distinct personality states accompanied by repeated episodes of dissociative amnesia.[1] For patients with DID, the perioperative period can be especially stressful, both physically and emotionally. Perioperative stress can lead to personality switching, dissociative amnesia, and disorder exacerbations and should therefore be minimized for these patients.

This case report discusses the administration of general anesthesia to a DID patient with 20 distinct personalities. Written consent was obtained from this patient regarding his inclusion in this case report.

CASE PRESENTATION

The patient was a 36-year-old man (height, 157 cm; weight, 64 kg; body mass index, 26) with a history of left cleft lip and palate planned to undergo a secondary alveolar bone graft from a tibial donor site. The patient's surgical history included cheiloplasty during infancy, palatoplasty at 1 year and 6 months of age, surgical correction of cryptorchidism at 5 years of age, and surgical intervention for a hemorrhagic gastric ulcer at 21 years of age. The patient reported no allergies nor any history of anesthetic complications. All surgeries prior to the onset of his DID were reported as being uneventful.

The patient was diagnosed with depression at the age of 21 following his gastric ulcer surgery. At the age of 33, he reportedly developed DID, involving 20 unique personalities in addition to his usual host personality (Table 1), that was triggered by extreme psychological stress after a motor vehicle accident that impacted his family.

The patient's personalities often switched before sleep or whenever his mental stress or anxiety was high. Alternate personalities commonly emerged prior to

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Table 1. List of Host and Alternate Personalities

Personality	*Name*	*Sex*	*Age, y*	*Appearance time*	*Description*
Frequently appearing personalities					
1*	X	M	36		Host personality
2	A	M	46		A dependable personality
3*	B	F	48	Night	A worrying personality; appeared before falling asleep
4	C	F	45		Kind-hearted with a sad past
5	D	M	15		Good at playing cards and Othello
6	E	F	44	Daytime	Responsible personality
7	F	F	31		Smart and caring
8*	X	M	7		7-year-old personality
9*	H	F	25	All day	Most frequently appearing alternative personality
10*	I	F	29		Took care during his recovery
Rarely appearing personalities					
11	X	M	30		
12	X	M	34		
13	J	M	17		
14	K	M	Unknown		
15	L	M	Unknown		
16	M	M	20		
17	N	F	37		
18	O	F	50		
19	P	F	20		
20	Q	F	18		
21	R	F	50		

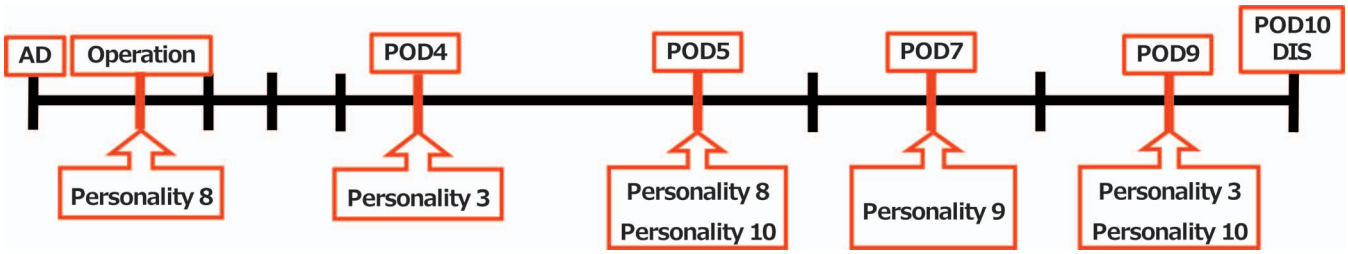
* Personalities that appeared during his hospitalization.

sleep, with the host and an alternate personality conversing while falling asleep. The patient's alternate personalities were not violent but had different facial expressions, gestures, and speech than his host personality. The timing and frequency of the appearances of his alternate personalities differed, with personality shifts typically lasting for only a few hours. Confirmation of his age and name was needed to identify his current personality (eg, "Are you Mr ——? Are you 36 years old?"). The patient's DID was being managed with regular oral medications and counseling. His reported medications included lansoprazole 15 mg daily for gastric ulcers; suvorexant 20 mg daily for insomnia; and vortioxetine 10 mg daily, chlorpromazine 25 mg daily, promethazine 25 mg daily, clonazepam 2 mg daily, blonanserin (an atypical antipsychotic used in Japan) 4 mg twice a day, and phenobarbital 30 mg twice a day for the management of his DID and depression.

The anesthesiologist had previously examined the patient 1 month before surgery, at which time his preoperative condition was unremarkable, with blood pressure of 119/90 mm Hg and a heart rate of 97 bpm. Information about the patient's general condition was obtained from his host personality, and his family was asked about how to manage his alternate personalities in detail. The day before the surgery, we interviewed the patient again and discussed the planned anesthetic management. His host personality was present at the time of examination, and informed consent for general anesthesia was obtained from that personality. At the request of the patient and his family, the number of staff in the operating room (OR) was to be minimal. A nurse was to accompany the patient, as he felt uneasy because of the risk of falling should an alternate personality switch occur. The patient's regular medications were continued preoperatively and resumed postoperatively to reduce the possibility of his mental condition worsening perioperatively.

The morning of surgery the patient took lansoprazole 15 mg and blonanserin 4 mg as usual. The patient's host personality was present upon awakening, but he switched to an alternate personality, a 7-year-old boy (personality 8; Table 1), around 6:30 AM. At 8:00 AM the anesthesiologist visited his room to confirm knowledge of the upcoming surgery, and the patient replied in a small, high-pitched voice, "My mom and dad told me about the surgery." The patient's 7-year-old boy personality remained present until anesthesia induction.

As the patient permitted peripheral intravenous (IV) access preoperatively, general anesthesia was induced rapidly after arrival to the OR with a target-controlled infusion (TCI) of propofol 3 μg/mL, remifentanil infusion 0.3 μg/kg/min, and bolus of rocuronium 50 mg. Orotracheal intubation with an 8.0 endotracheal tube was easily performed after direct laryngoscopy. General anesthesia was maintained with a propofol TCI of 1.3 to 2 μg/mL, sevoflurane 0.8%, oxygen 1 L/min, air 2 L/min, and remifentanil infusion 0.05 to 0.2 μg/kg/



Perioperative timeline. Several of the patient's alternative personalities emerged throughout the course of his hospital stay, but his host personality returned within a few hours each time. AD indicates admission day; POD, postoperative day; and DIS, discharge.

min, in addition to fentanyl (total dose 200 μg) and rocuronium (total dose 80 mg) administered as needed. The propofol TCI was adjusted to achieve bispectral index (BIS) values around 40 to 60 during surgery. Prior to extubation, neuromuscular blockade was reversed with sugammadex 150 mg, and full recovery was confirmed using neuromuscular monitoring.

The patient was extubated without incident after confirmed recovery of consciousness, spontaneous respirations, and return of voluntary movements. There was no delayed awakening or emergence delirium. Immediately after emergence, the patient was able to confirm his name and age, establishing the presence of his host personality. The patient's cardiovascular and respiratory vital signs were stable, so he was discharged from the OR. After returning to the perioperative holding area, we interviewed the patient about having any memories of entering the OR, which he denied. The patient's postoperative pain was well managed with oral acetaminophen, as he was unable to use loxoprofen.

Discharge time at our hospital is influenced by healing of the surgical site and whether patients can effectively ambulate.[2] Postoperatively, tibial bone graft patients must wait for recovery of mobility using either a wheelchair or a walker.[2] The patient used a wheelchair on postoperative day 1 and a walker on postoperative day 2, progressing well with no changes in personality. However, on postoperative day 4 the patient's personality switched to that of a 48-year-old woman (personality 3). On postoperative day 5, when he was told to stop using a walker, he switched back to personality 8 and to that of a 29-year-old woman (personality 10). Next, on postoperative day 7 he again changed personalities, to that of a 25-year-old woman (personality 9). Finally, on postoperative day 9, which was 1 day prior to discharge, the patient switched to personalities 3 and 10 (Table 1; Figure).

No psychiatric treatment was given for any of these alternate personalities, which lasted a few hours. Between these personality switches, he would return to his host personality, which was present for most of his hospital stay. Similar to his lack of preoperative memories, the patient had no recollection of his alternate personalities' experiences once his host personality returned. The patient was discharged on postoperative day 10 for a total hospital stay of 12 days, as is common in our hospital system.

DISCUSSION

DID is characterized by multiple personalities, personality switching, and repeated episodes of dissociative amnesia.[1] The causes of DID are typically thought to be related to traumatic childhood events or abuse, and the alternate personality states are thought to arise to protect the patient's psyche from traumatic events.[1] DID has been reported in a number of studies to be more common in younger individuals.[1,3] In a report of 468 patients hospitalized with DID in the United Arab Emirates, 318 (68%) were younger than 25 years of age.[4]

Reports on general anesthesia for patients with DID are rare,[5–8] although personality switching during hospitalization and after general anesthesia has been reported.[6,7] Concerns related to general anesthesia include refusal of medical treatment by alternative personalities, psychological shock before and after general anesthesia due to personality changes, delayed emergence due to interactions with regular psychiatric medications, and side effects of those medications.

In this case, we paid attention to 3 points when planning and performing general anesthesia: (1) obtaining consent for general anesthesia smoothly without communication difficulties; (2) minimizing preoperative psychological stress and smoothly inducing general anesthesia; and (3) preventing an exacerbation of the patient's mental state due to delayed emergence or emergence delirium.

The patient had the right and ability to make his own medical decisions. For patients with DID, it has been reported that it is necessary to obtain consent not only from the host personality but also from all alternative personalities.[6] However, it may be difficult to obtain consent from all personalities because of the varying

Table 2. Patient's Regular Medications and Potential Anesthetic Implications*

Medication	T_{max}, *h*	$t_{1/2}$, *h*	*Potential anesthetic concern or effect**
Suvorexant	1-3	10 ± 1	Orexin receptor inhibition
Vortioxetine	6-14	67.6	Central nervous system inhibition via 5-HT_{1A} receptor agonistic activity
Blonanserin	2	67.9 ± 27.6	Sedation via α_1 receptor antagonism
Chlorpromazine	3.2 ± 0.8	11.7 ± 4.7	Sedation via α_1 receptor antagonism
Phenobarbital	1.4 ± 0.5	119 ± 18.6	$GABA_A$ receptor–mediated sedation
Clonazepam	2	27	$GABA_A$ receptor–mediated sedation
Promethazine	2.7 ± 0.6	12.7 ± 2.4	Sedation via antihistaminergic activity

* Enhanced anesthetic effects are present for all listed medications.
† 5-HT_{1A} = 5-hydroxytryptamine (1A) receptor.
‡ $GABA_A$ = gamma-Aminobutyric acid (A) receptor.

frequency and duration of their appearances. In this case, none of the patient's alternate personalities were ever present during the preoperative consultations, so anesthesia consent was obtained only from the host personality. Well before the date of the procedure and with the cooperation of the host personality and his family, we asked that all personalities understand they would undergo surgery and general anesthesia. If a switch in personality occurred before induction of general anesthesia, we planned to obtain consent again. If the alternate personality did not consent to the surgery or anesthesia, the surgery would be cancelled.

In this case, personality 8 (a 7-year-old boy) emerged on the day of surgery. Because that personality was cooperative and fully understood the necessity of the surgical operation and anesthesia, we decided to obtain oral consent only. In retrospect, it would have been ideal to have obtained written consent from this personality as well. Depending on the specific alternate personality, written consent may be required.

It was thought that the patient's alternate personality emerged because of psychological stress, which was easily predicted in advance. We believe that presence of staff immediately after emergence reduced anxiety and prevented further personality switching as much as possible. We also tried to avoid putting a psychological burden on the patient by minimizing the number of people who entered the OR upon his arrival and during emergence and avoiding loud noises during his hospital admission. When the 7-year-old boy personality emerged, we tried to eliminate stress as much as possible by using topical anesthetic, which permitted the placement of peripheral IV access while the patient was awake. In summary, it is possible to smoothly induce anesthesia in patients with DID by preparing the environment and reducing preoperative stress as much as possible, particularly if an alternate personality has emerged due to current stressors.

With respect to delayed emergence, there have been reports that DID patients have reduced volatile and IV anesthetic requirements (~50%-80%) compared to healthy adults.[9] There have also been reports of delayed emergence due to possible interactions with several of the patient's regular medications (Table 2).[9] Although the patient held all his routine medications except the lansoprazole and blonanserin, most have prolonged half-lives and could have enhanced effects of the anesthetic agents or caused added sedative effects. Rather than discontinue his routine medications and risk worsening his DID symptoms, we elected to continue his normal medications and carefully control the anesthetic depth with short-acting agents with clean emergence profiles to achieve an optimal level of anesthesia and avoid delayed emergence and recovery. Furthermore, we used a BIS monitor intraoperatively to help maintain an optimal depth of anesthesia, preventing excessive anesthetic administration and delayed arousal.

It was possible that the patient's personality upon emergence and recovery would not be the same as his personality at the time of induction. As the patient reported dissociative amnesia whenever an alternate personality was present, it was anticipated the patient could become confused, overly stressed, and excited if a personality change occurred upon awakening, leading to an exacerbation of his mental state. A combination of propofol, sevoflurane, and remifentanil was administered to help avoid excessive drug accumulation, delayed arousal, and emergence delirium. This combination not only was effective at maintaining general anesthesia but also allowed for the use of lower total drug dosages compared with monotherapy.[10]

In addition to being a sedative, propofol inhibits the cough reflex and can suppress coughing caused by emergence from anesthesia and stimulation from an endotracheal tube.[11] The patient in this case did not cough and awoke calmly without excitement. If the patient became agitated or demonstrated emergence delirium prior to extubation, we planned to reinduce the patient with propofol and perform a deep extubation

after the return of spontaneous ventilation. If such an event occurred, we felt that allowing him to emerge from anesthesia in his ward room rather than in the OR might help prevent him from becoming agitated upon awakening.

There have been reports of new personalities developing because of perioperative stress, which can worsen DID symptoms.[12] Because our hospital lacks a psychiatry department, we decided to consult the patient's family psychiatrist if a new personality or uncontrollable deterioration of the patient's mental state was observed. However, no personality switch was noted after emergence from anesthesia through postoperative day 3, and no new personalities emerged throughout his hospital stay. The patient did experience several personality changes that likely occurred as a result of increased stress (eg, being instructed to stop using a walker or preparing for discharge).

DID patients often have other psychiatric comorbidities like generalized anxiety disorder and are more susceptible to anxiety and stress.[3,8] This patient's personality switching was likely caused by anxiety before surgery and his concerns postoperatively about falling when walking alone. We discovered the patient had a strong anxiety about "falling down when walking alone" because that was what his alternate personality frequently told the nurse. We consequently tried to reduce his anxiety by talking and accompanying him during his walks.

CONCLUSION

We successfully performed general anesthesia for a patient with DID by managing patient anxiety, minimizing environmental stimulation, and avoiding emergence delirium or any delays in awakening by using a combination of short-acting anesthetic agents with clean emergence profiles. DID patients are highly stressed during the perioperative period and are more likely to experience personality switching as a result. Reducing stress throughout the perioperative period is most important to prevent a DID exacerbation. It is critical to discuss with DID patients what elements may cause them anxiety and to anticipate and properly manage situations in which DID patients may feel overly stressed.

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Alternative Technique for Nasotracheal Intubation Using a Flexible Fiberoptic Scope

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In oral maxillofacial surgery, the endotracheal tube (ETT) is often inserted nasotracheally to provide surgeons a better view and easier access to the oral cavity. Use of a flexible fiberoptic scope is an effective technique for difficult intubation. While the airway anatomy can be observed as the scope is advanced, the ETT tip cannot be observed with the traditional method. It is occasionally difficult to advance the ETT beyond the glottis as impingement of the ETT tip may occur. We devised a new nasotracheal intubation technique using a fiberoptic scope. In this novel technique, the ETT and fiberoptic scope are inserted into the pharyngeal space separately through the right and left nasal cavities. This permits continuous observation of the glottis as the ETT is advanced into the trachea. The main advantage of this technique is that the ETT tip is visualized as it is advanced, which helps avoid impingement of the ETT. If resistance is noted, the ETT can easily be rotated or withdrawn without causing laryngeal damage, leading to safe and smooth intubation. This novel technique allows advancement of the ETT under continuous indirect vision, thus minimizing contact of the ETT with the laryngeal structures and aiding in unhindered passage into the glottis.

Key Words: Nasotracheal intubation; Flexible fiberoptic scope; Anesthetic technique.

Recently, video laryngoscope devices, such as the Pentax-AWS (Pentax Corporation), have become more widely used for difficult intubations.[1–3] Improved visualization often facilitates easy placement of the endotracheal tube (ETT) into the trachea. However, use of these devices can be impossible in some patients with significant limited mouth opening (eg, infection, trismus, temporomandibular joint ankylosis) as these devices require sufficient space for the blade to be inserted into the mouth. Moreover, the blades of these devices should not be inserted into the mouth in some cases of oral cancer as their use may stimulate bleeding or inflammation of the friable tissues. Therefore, intubation using a flexible fiberoptic scope is a commonly used technique for these types of difficult airway cases.[4,5]

In oral and maxillofacial surgery, the ETT is often inserted nasotracheally to provide a better view for surgeons and to allow easy access to the oral cavity.[3] In our clinical practice, the nasotracheal tube is first inserted into the pharynx through the nares and nasal cavity. The flexible fiberoptic scope is then inserted through the ETT, and the scope tip is carefully directed past the glottis and into the trachea under indirect vision. Once intratracheal positioning of the scope is confirmed, the ETT is advanced blindly into the trachea, guided by the fiberoptic scope. By advancing the tip of the fiberoptic scope under indirect vision, we can observe the pharyngeal, laryngeal, and tracheal anatomy (Figure 1a). Successful placement of the ETT within the trachea is visually confirmed with the scope (Figure 1b). However, the tip of the ETT cannot be observed as it is advanced along the length of the fiberoptic scope using this blind technique, which may lead to difficulties if impingement of the ETT tip occurs. We have devised a new nasotracheal intubation technique that addresses these issues.

METHODS

In this novel technique, the ETT is carefully advanced through the nasopharynx and into the posterior

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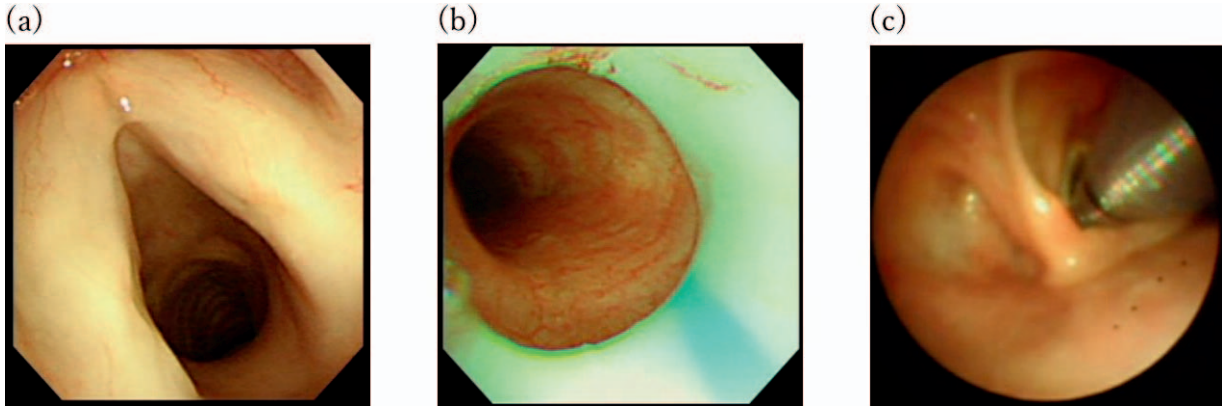

Figure 1. Fiberoptic view during nasotracheal intubation using the traditional fiberoptic scope technique (a, b) and our new technique (c). (a) Indirect visualization of the glottis prior to advancement of the endotracheal tube (ETT). (b) Tip of the ETT as it is advanced blindly along the fiberoptic scope. Passage through the glottis cannot be visually confirmed, so the ETT could become impinged upon on a trachea ring or laryngeal anatomy.(c) Advancement of the ETT through the glottis under continuous indirect visualization.

oropharynx while the flexible fiberoptic scope is inserted through the contralateral side of the nasal cavity. This allows the ETT and the scope to be advanced separately, and the glottis can be continuously observed using the scope as the ETT is advanced between the vocal cords into the trachea. The main advantage of this technique is that the ETT tip can be observed at the glottis as it is advanced to help identify and avoid impingement upon the laryngeal structures (ie, vocal cords). Insertion of the ETT is indirectly monitored using the flexible fiberoptic scope with full view of the larynx (Figure 1c). This technique allows advancement of the ETT under continuous indirect vision, thus minimizing contact of the ETT with the laryngeal structures and aiding in unhindered passage through the glottis.

DISCUSSION

There are times when fiberoptic intubation can be difficult. Induction of general anesthesia causes relaxation of the airway musculature and can lead to collapse of the airway as the soft palate, tongue, and epiglottis approximate the posterior pharyngeal wall. This leaves little air space left in the pharynx to successfully maneuver the scope tip and locate the glottis.

Furthermore, it is possible that tracheal intubation fails despite successful insertion of the fiberoptic scope into the trachea. The ETT can deviate away from the path of the scope as it is advanced into the trachea, enabling the ETT tip to become lodged on the laryngeal structures. This can lead to difficulty successfully advancing the ETT over the fiberoptic scope and into the trachea. Moreover, if care is not taken to ensure the fiberoptic scope remains within the trachea, the ETT could cause displacement of the scope upon advancement and be inadvertently inserted into the esophagus despite the scope's correct initial placement in the trachea. Difficulty advancing the ETT has been reported to occur in 20%–90% of patients.[4–6] The size of the tongue and length of the epiglottis have been correlated with the incidence of ETT impingement. Deformity or distortion of the upper airway can also obstruct passage of the ETT over the fiberoptic scope.[4,7] Repeated attempts to advance the ETT over the fiberoptic scope and into the trachea might increase the risk of injury to the glottic tissues. Several maneuvers have been proposed to solve this problem, such as thrusting the jaw forward or rotating the ETT, which might reduce resistance by releasing the ETT tip that is impinging on the laryngeal structures.[6–8]

It is not necessary to pass the fiberoptic scope through the nasal cavity (nasolaryngeal insertion) to visualize the ETT tip. Orolaryngeal insertion of the scope might be beneficial to permit visualization of the ETT tip without risking nasal bleeding. However, we believe that nasolaryngeal insertion of the fiberoptic scope allows easier passage through the nasal cavity and improved observation of the ETT at the same angle as compared with orolaryngeal insertion. The view obtained using the fiberoptic scope is usually more stable when nasolarygneal insertion is used as the scope is somewhat supported by the nasal anatomy. We feel this approach positively affects the success rate of tracheal intubation and might reduce the risk of postoperative sore throat.[6,10]

Occasionally, it might be difficult to manipulate the ETT and direct it into the trachea. For example, the ETT may become stuck on a tracheal ring or the vocal cords despite the perfect view for intubation. In such a

situation, the operator can ask for assistance visualizing the larynx and/or intubating. To help avoid this situation, we have found that 2 technical options are useful: (1) insert 1 scope into the ETT and a second scope into the contralateral side of the nasal cavity, or (2) insert an introducer (ie, tube exchanger) into the ETT while the ETT tip is visualized with the scope. Either approach permits easier manipulation of the ETT tip and passage through the glottis. Moreover, we have also solved this problem by rotating and/or withdrawing the ETT without laryngeal damage, which led to safe and smooth intubation.[7]

We have used this technique effectively for intubating conscious and unconscious patients. Care must be taken not to damage the pharyngeal tissues when this technique is utilized after induction of general anesthesia due to the potential for reduced pharyngeal air spaces. For awake intubations, the use of sedatives and local anesthetics are needed to maintain spontaneous ventilation, facilitate patient cooperation, and to enable the patient to tolerate passage of the fiberoptic scope to facilitate intubation.[8]

Generally, nasotracheal intubation under direct vision requires alignment of the oral cavity, pharynx, and larynx (ie, the 3 airway axes), and the glottis must be visible.[9] However, aligning these axes is not as important in this technique. Instead, it is more important to secure a large pharyngeal space for maximal visualization of the field while operating the scope for intubation by placing the patient in the supine position without a pillow. In addition, emergency airway equipment, including a video laryngoscope and surgical airway/tracheostomy kit, should be readily available for use in case the procedure fails, and the patient's airway is lost.

CONCLUSION

This new technique allows advancement of the ETT under continuous indirect vision with a flexible fiberoptic scope, thus minimizing contact or impingement of the ETT with the laryngeal structures and aiding in unhindered passage through the glottis. We are confident this novel approach should be considered for use in all nasotracheal intubation cases.

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A Case of Wide QRS Tachycardia After the Local Administration of Epinephrine to Reduce Bleeding During General Anesthesia

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We report a case of wide QRS tachycardia or ventricular tachycardia with a pulse after the administration of epinephrine under general anesthesia. After induction and achieving a sufficiently deep plane of general anesthesia, gauze soaked in a 1:100,000 epinephrine solution was applied to the patient's nasal mucosa and 1% lidocaine with 1:100,000 epinephrine was administered via intraoral infiltration. Several minutes after the start of surgery, the patient's blood pressure and heart rate suddenly increased and a wide QRS tachycardia was observed on the electrocardiogram, which then reverted to a normal sinus rhythm. According to the past reports, similar arrhythmias have occurred after administration of epinephrine in the head and neck. These findings suggest that anesthesia providers must be aware of the risks associated with epinephrine and local anesthetic use, particularly in the head and neck region.

Key Words: Epinephrine; Sevoflurane; Arrhythmia; Wide QRS tachycardia; Ventricular tachycardia with a pulse.

CASE REPORT

This case report focuses on a 77-year-old female (height, 154 cm; weight, 41.5 kg; body mass index, 17.4 kg/m^2) who underwent left partial maxillectomy for a malignant gingival tumor diagnosed as squamous cell carcinoma. The patient had previously been diagnosed with suspected angina 30 years prior although no detailed cardiac examination was performed, and she denied any history of chest pain since. No other systemic illnesses were reported, and preoperative laboratory findings of the patient were normal. A normal sinus rhythm was observed on the patient's electrocardiogram (ECG).

In the operating room, the patient's initial arterial blood pressure (ABP) via noninvasive blood pressure cuff and heart rate (HR) were 141/56 mm Hg and 81 bpm, respectively. General anesthesia was induced using fentanyl 50 μg, propofol 60 mg, and rocuronium 40 mg. The patient was nasally intubated, and an invasive arterial catheter was placed in the right radial artery. Anesthesia was maintained using sevoflurane 1.2% with oxygen 1 L/min and air 5 L/min plus a continuous infusion of remifentanil (0.1–0.2 μg/kg/min). Prior to the start of the surgical procedure, gauze soaked in a solution containing saline and 1:100,000 epinephrine (saline 100 mL + 1:1000 epinephrine 1 mL) was applied to the patient's nasal mucosa to minimize surgical bleeding from the nasal cavity. After confirming a negative aspiration, the surgeon then injected 10 mL of 1% lidocaine containing 1:100,000 epinephrine (total dose: lidocaine 100 mg and epinephrine 0.1 mg) into the left maxillary gingival mucosa via local infiltration. Approximately 7 minutes after placement of the epinephrine-soaked gauze and 2 minutes after injecting the local anesthetic, fentanyl 50 μg was administered intravenously for intraoperative analgesia, and the surgery was started. The patient's ABP per the right radial arterial line and HR were 126/78 mm Hg and 78 bpm at the start of surgery. However, 3 minutes after starting surgery, her ABP and HR suddenly increased to 187/76 mm Hg and 123 bpm, respectively, and the ECG showed a wide QRS complex tachycardia that was diagnosed as ventricular

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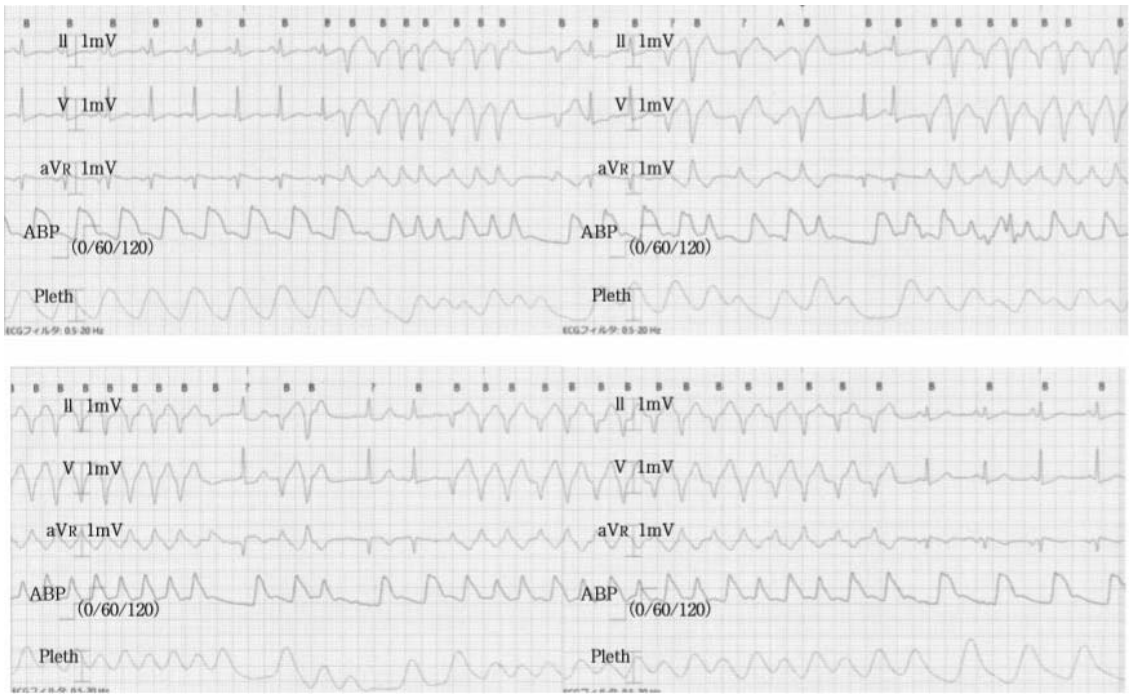

Figure 1. Transient (~22 seconds) ventricular tachycardia with a pulse. Electrocardiogram (leads II, V5, aVR), arterial blood pressure, and pulse oximetry waveforms during the wide QRS tachycardia event.

tachycardia with a pulse (Figure 1) as established by the continued presence of pulse oximeter and ABG waveforms. The surgery was interrupted to remove the epinephrine-soaked gauze and prepare the patient for use of a defibrillator in the event her cardiovascular status further deteriorated. The episode of ventricular tachycardia with a pulse persisted intermittently for 22 seconds. Thereafter, the patient spontaneously recovered to a normal sinus rhythm with a gradual decrease in ABP (100–120/45–60 mm Hg) and HR (80–90 bpm) coincident with adequate depth of anesthesia, and the surgery was resumed with no further abnormalities observed.

DISCUSSION

Previous studies have reported epinephrine-induced arrhythmias for surgeries involving the head and neck region under general anesthesia using sevoflurane or desflurane even though these agents are less likely to cause an arrhythmia compared with other inhalational anesthetics like halothane.[1–4] This is thought to be attributed to rapid absorption of epinephrine due to the presence of abundant blood flow in this region.[1] The wide QRS tachycardia or ventricular tachycardia with a pulse observed in the current case was presumed to be caused by a large amount of epinephrine entering the blood from 2 potential sources. Although an accidental intravascular injection could have occurred during injection of local anesthetic, it was deemed unlikely due to the timing of the wide QRS tachycardia onset relative to the injection.[1] Instead it was felt that the epinephrine dose delivered by the gauze was likely excessive as the exact amount contained in the gauze and ultimately absorbed through the patient's nasal mucosa was unknown. Administration of epinephrine requires care and attention to all potential sources of uptake to prevent inadvertent overdose.

The patient was referred for detailed cardiovascular examination postoperatively due to previous reports of healthy patients developing ventricular tachycardia after administration of epinephrine to the nasal mucosa who were later diagnosed with variant angina.[2,3] Unfortunately, the patient in this case decided against pursuing a referral and evaluation with cardiology.

CONCLUSION

Wide QRS tachycardia or ventricular tachycardia with a pulse was transiently observed in a patient under general anesthesia following topical nasal mucosal application of epinephrine-soaked gauze and intraoral infiltration of lidocaine with epinephrine for local anesthesia. Anesthesia providers must be aware of the risks associated with epinephrine and local anesthetic use, particularly in

the head and neck region, and consider all potential sources for epinephrine uptake.

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Implications of Electronic Cigarettes on the Safe Administration of Sedation and General Anesthesia in the Outpatient Dental Setting

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Today the number of electronic cigarette users continues to rise as electronic cigarettes slowly, yet steadily overtake conventional cigarettes in popularity. This shift is often attributed to the misconception that electronic cigarettes are "safer" or "less dangerous" than conventional cigarettes. Recent studies have shown that electronic cigarettes are far from safe and that the inhaled agents and byproducts within vaping aerosols can have adverse effects on systemic and oral health like combustible tobacco products. The first electronic cigarettes were originally introduced as a tool for smoking cessation. However, newer iterations of electronic cigarette devices have been modified to allow the user to consume tetrahydrocannabinol (THC), the psychoactive component of cannabis, in addition to nicotine. As the popularity of these devices continues to rise, the number of patients seeking dental treatment who also consume electronic cigarettes will too. This article aims to shed light on the deleterious effects electronic cigarettes can have on systemic and oral health, as well as the special considerations for sedation and anesthesia providers treating patients who use electronic cigarettes.

Key Words: Electronic cigarette; Vaping; Oral surgery; Dentistry; General anesthesia; Sedation.

Vaping devices, also known as electronic cigarettes (e-cigarettes) or electronic nicotine delivery systems, were first introduced to the US market in 2007 as aids for smoking cessation. Use of these devices rapidly grew in popularity as users perceived them as safe alternatives to conventional cigarettes and other smoked tobacco products.[1] When initially introduced, the effects that e-cigarettes had on one's health were unknown, and the number of users has continued to grow over time. Now there are many prospective and retrospective studies documenting the deleterious systemic effects of e-cigarette use.[2] An area of interest for providers of sedation and general anesthesia is the effect of e-cigarettes on multiple organ systems. Just like conventional cigarette users, patients who use vaping devices often require a more extensive preoperative workup and potentially alternative approaches to safely provide deep sedation or general anesthesia in the outpatient dental setting.

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HISTORY AND BACKGROUND

Electronic cigarettes are composed of a battery, a reservoir for holding a vaporizable solution that typically contains nicotine, a heating element or an atomizer, and a mouthpiece through which the user inhales or "puffs" (Figures 1 and 2).[3] Electronic cigarettes create aerosols when the user draws in air through the mouthpiece. This triggers the device to begin drawing liquid solution from the tank or reservoir and pass it over the internal heating element. The liquid is then vaporized by the heating element, which operates at temperatures ranging between 100°C and 300°C

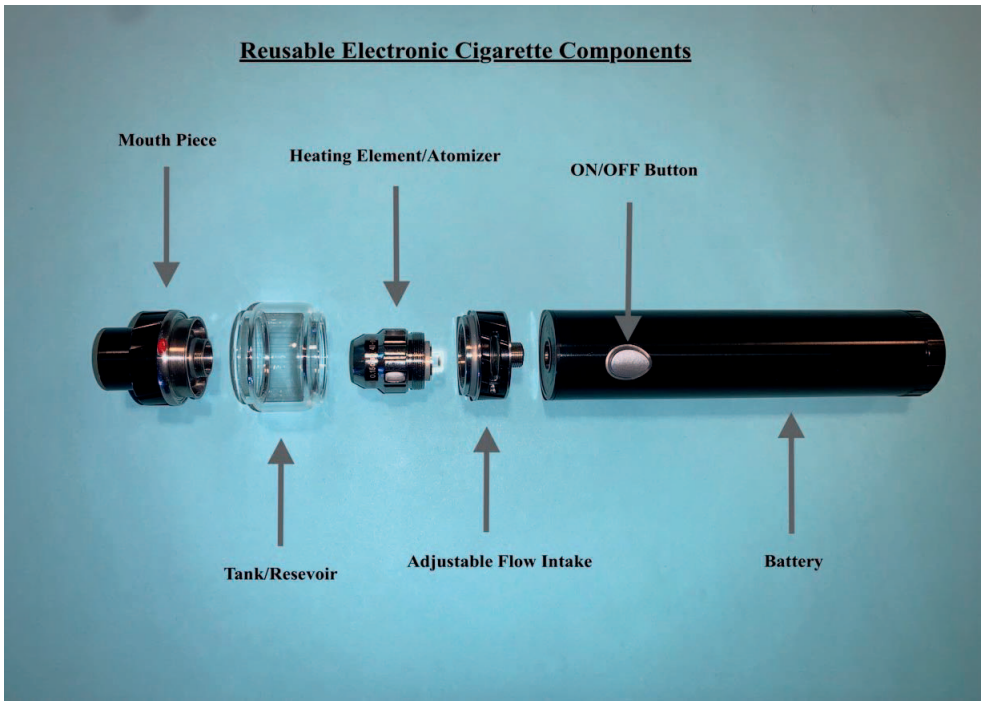

Figure 1. Reusable electronic cigarette components. Reusable e-cigarettes are composed of a plastic or glass tank which allows the user to store a greater volume of e-liquid. The heating element is typically an atomizer which allows for greater generation of aerosols. Reusable e-cigarettes contain a larger battery compared with disposable ones. A larger power supply to the heating element allows for a greater volume of aerosol to be generated with each puff.

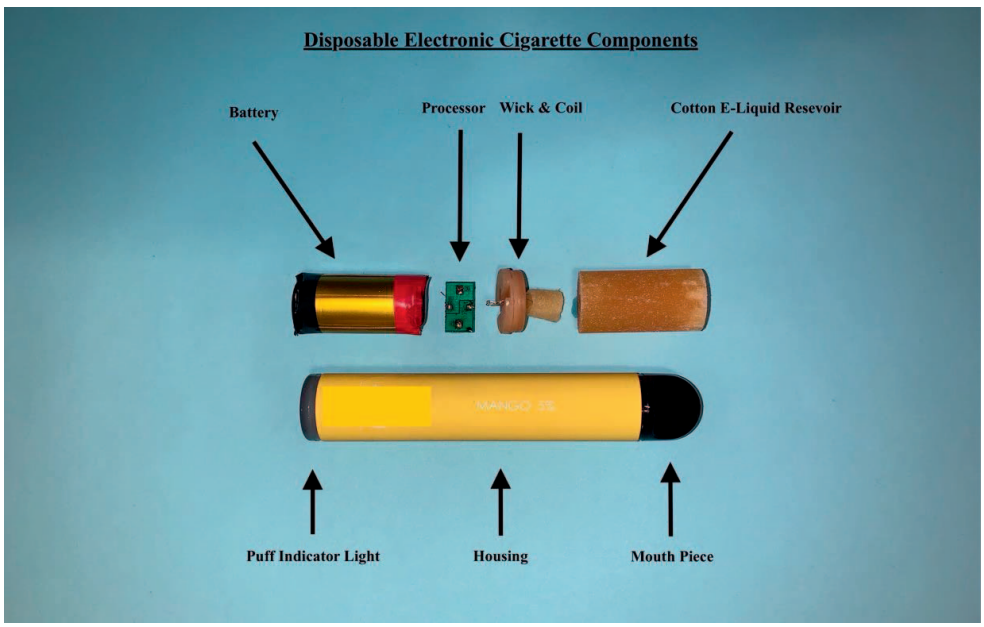

Figure 2. Components of a disposable electronic cigarette. Disposable e-cigarettes do not contain a tank and instead store their e-liquid in a saturated piece of cotton. Aerosols are generated by a rudimentary wick and coil which is heated by a low voltage battery. The processor recognizes when the user is taking a puff and triggers the battery to supply power to the coil. The processor is set to a predetermined number of puffs. The device will stop generating aerosols once that number is reached or the battery runs out of power, whichever comes first.

depending on the device's construction and power output. As the device heats the liquid solution (often called "e-liquid" or "e-juice"), an aerosol or vapor is produced that is inhaled by the user.

Upon their introduction, electronic cigarettes were novel devices with no literature to document their safety. Subsequently, electronic cigarette manufacturers were able to market their products to the public as "safe" since they did not contain any tobacco nor used combustion to produce aerosols. Most of the well-known effects of tobacco are understood from combustion reactions rather than the vaporization of "e-liquids" with electronic cigarettes.[4] Due to the quantitative lack of published research on vaporization products, the widespread misconception that using vaping devices is safer than smoking conventional cigarettes permeated its way into the mainstream.

The largest and most rapidly growing demographic of e-cigarette users are teenagers and young adults who view using these devices as benign compared with conventional cigarettes.[5] The adoption of electronic cigarettes over conventional cigarettes in this patient population is also appealing because many e-liquids are flavored (eg, fruit, cotton candy, or chocolate). The US Centers for Disease Control and Prevention (CDC) has reported an increase in the use of electronic cigarette devices among both US middle and high school students, and the proportion of young adults (18–24 years) who are current e-cigarette users exceeds that of older adults (>25 years).[6] Additionally, the CDC reported the use of electronic cigarette devices by teenagers increased from 1.5% in 2011 to 20.8% in 2018, surpassing conventional cigarette use in this population.[7] The growing popularity of electronic cigarettes within younger populations is an important consideration for providers of sedation and general anesthesia for dentistry since third molar extraction, one of the most common outpatient surgeries performed in office-based settings, typically occurs during the second and third decade of life.[8] As such, the usual preoperative assessments that are performed in traditional smokers should ideally include users of electronic cigarettes.

PREOPERATIVE ASSESSMENT CONSIDERATIONS

Oral Effects

A commonly overlooked aspect of vaping devices are their effects upon the oral cavity. Many users believe inhaling aerosols from electronic cigarettes has minimal sequelae on the oral cavity due to the aerosols being generated through a noncombustion reaction, which renders the "vapor" smokeless. Since there is no combustion, users often discount the many epidemiological studies that have shown a positive correlation between the use of combustible tobacco products and increased risks of periodontitis, oral cancer, tooth loss, and dental implant failures.[9] Although the vapor is produced through a noncombustion reaction, there are many dangers associated with the generation of aerosols from electronic cigarette devices. Recent studies are beginning to highlight the harmful effects of electronic cigarettes on both the hard and soft tissues of the oral cavity.

The elevated temperatures produced during vaporization facilitate transfer of heavy metals with high atomic density and toxicity to humans (eg, nickel, cadmium, chromium, and lead), from the coil into the e-liquid.[10] In addition to the presence of heavy metals in electronic cigarette aerosols, other known carcinogens and mutagens like formaldehyde, acetaldehyde, and acrolein have been recorded in the vapor produced by the device.[11]

Consumption of and exposure to these heavy metals and carcinogens has detrimental effects on the periodontium of the oral cavity. Like the reactive oxygen species from cigarette smoke and its deleterious effects on the periodontium and increased risk of periodontitis, recent research has shown that the noxious chemicals found in e-liquid aerosols causes increased oxidative and carbonyl stress with inflammatory cytokine release in human periodontal ligament fibroblasts.[12] Additionally, increased oxidative stress and inflammatory cytokine release can lead to gingival recession and crestal bone loss.[13] The chemicals found in e-liquids and e-cigarette aerosols are also detrimental to the health and long-term prognosis of the osseointegration of dental implants. The use of electronic cigarette devices increases the levels of tumor necrosis factor-α and interleukin-1β in peri-implant sulcular fluid causing an increased local inflammatory response around the implant, which leads to bleeding with probing, increased probing depths, and ultimately, implant failure.[14]

E-liquids with or without nicotine also demonstrated cytotoxic and genotoxic effects on human oropharyngeal mucosa.[10] Oral epithelial cell lines that have been exposed to electronic cigarette aerosols have shown significantly reduced cell viability and increased rates of apoptosis and necrosis, regardless of whether the e-liquid contained nicotine.[15] The toxicants in the aerosols appear to be retained in intraoral fluids and tissues at levels often approximating 90% of baseline levels found originally in the inhaled aerosol. These water-soluble reactive toxins can challenge the oral cavity constituents, potentially contributing to alterations in the native oral microbiome and host cells critical for maintaining oral

homeostasis.[10] Disruption of the normal oral flora may further perpetuate the user's risk of developing periodontitis and/or opportunistic oral infections. Additionally, it has been found that nicotine in e-liquids facilitates increased adhesion of *Streptococcus mutans* on intraoral hard tissues, doubling the production of oral biofilms and increasing the caries potential.[2] Like combustible tobacco products, electronic cigarettes can clearly contribute to the development of periodontitis, tooth loss, implant failure, and oropharyngeal cancer.

Cardiovascular Effects

Although vaping devices were originally touted to be safe in comparison to conventional cigarettes, recent literature has begun to highlight how electronic cigarettes can negatively impact the cardiovascular system like conventional cigarette use. A hallmark finding in cardiovascular diseases is heightened platelet aggregation and increased risk of thromboses. In a study conducted by Hom et al,[16] an increase in the platelet aggregation rate and percentage aggregation was noticeable in as little as 15 minutes after exposure to vaping aerosols, independent of whether the aerosol contained nicotine. The platelet aggregation rate continued to rise, peaking at 1 hour after initial aerosol exposure. The enhanced platelet aggregation is believed to be caused by the inhalation of fine particulate matter, which is a byproduct of electronic cigarette aerosol generation.[16]

E-cigarettes can negatively affect a patient's preoperative vital signs. Acute inhalation of aerosols from an electronic cigarette can increase a patient's heart rate and elevate their systolic blood pressure.[17] An increase in blood pressure after acute inhalation of vaping aerosols can partly be attributed to nicotine within some e-liquids. Nicotine activates the renin-angiotensin-aldosterone system by upregulating angiotensin converting enzyme, which converts angiotensin I to angiotensin II and thus increases blood pressure, stimulates the release of norepinephrine, and promotes fluid retention. These changes can lead to a 79% greater risk of an acute myocardial infarction over non-nicotine vaping users and individuals who never use any form of electronic or conventional cigarettes. Overall, a chronic electronic cigarette user has a 1.7× greater chance of sustaining a myocardial infarction over the course of their life.[18,19]

When propylene glycol and glycerin in e-liquids are heated, they subsequently degrade and form carbonyl compounds. These compounds include the following: acrolein, formaldehyde, and acetaldehyde. Carbonyl compounds have been found to cause oxidative stress and inflammation throughout the body, specifically in the cardiovascular system.[20] Exposure to acrolein is linked to an increase in the indices of platelet activation, such as the formation of platelet-leukocyte aggregates in the blood, increased plasma PF4 levels, and increased platelet-fibrinogen binding. This indicates inhalation of electronic cigarette aerosols can predispose the user to thrombotic events.[21] In addition to increasing the risk of thrombotic events, the fine particulate matter found in electronic cigarette aerosols has been linked to global vascular endothelial dysfunction. Altered vascular endothelial permeability can lead to the development of atherosclerosis, hypertension, and eventual heart failure.[22]

According to the CDC, men are more likely than women to have ever tried vaping devices. When analyzing the gender distribution of current electronic cigarette users, men are twice as likely as women to be current users.[23] Interestingly, the use of electronic cigarette devices has been linked to male erectile dysfunction, and the link was found to be independent of the male's age and cardiovascular disease status.[24] Erectile dysfunction in vaping device users is thought to be caused by impaired vasodilation and reduced penile circulation due to the elevated nicotine levels found in vaping aerosols. Nicotine is not thought to be the only cause of erectile dysfunction in male electronic cigarette users. Research shows e-liquids with and without nicotine can cause a reduction in circulating testosterone levels, which leads to reduced mRNA expression of steroidogenesis enzymes responsible for normal erectile function.[25]

Respiratory Effects

There is an ever-growing body of literature from in-vitro animal and human studies documenting the deleterious effects of inhaling vaping aerosols on the respiratory system. One of the most widely publicized consequences of chronic electronic cigarette use is bronchiolitis obliterans, more commonly known as "popcorn lung." The nickname arose in the early 2000s after 8 cases of severe bronchiolitis obliterans were recorded in workers at a microwave popcorn factory. The disease cluster was later traced back to the inhalation of volatile flavoring agents used in the production process. The identified aerosolized flavoring agents were diacetyl (2,3-butanedione) diketone, and 2,3-pentanedione and are used in the manufacturing process to increase aroma and flavor intensity.[26] These same flavoring agents are also regularly found in e-liquids. Likewise, the pathophysi-

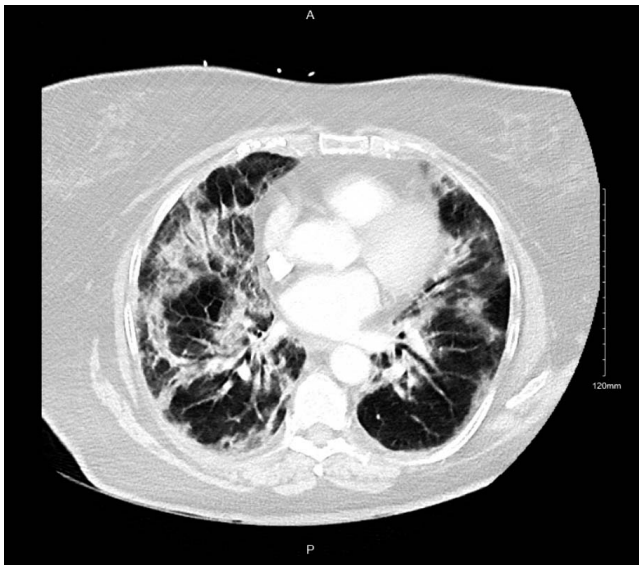

Figure 3. Bronchiolitis obliterans or "popcorn lung." Axial view of a CT chest in a patient who chronically used electronic cigarette devices, suffering from bronchiolitis obliterans. Image provided courtesy of Dr Jeremy S. Breit, MD.

ology of the popcorn lung secondary to vaping is believed to be initiated by the epithelial damage caused by diacetyl (2,3-butanedione) diketone and 2,3-pentanedione.[27] The airway surface liquid and mucociliary clearance is regulated in epithelial cells through absorption of Na^+ and Cl^- secretion in epithelial cells. These chemicals disrupt the transepithelial Na^+ transporters, which causes the proliferation of granulation tissue within the bronchiolar epithelium leading to complete and partial obstruction of the bronchioles (Figure 3).[28] Prolonged exposure to diacetyl (2,3-butanedione), diketone, and 2,3-pentanedione can lead to fixed airflow obstruction, gas exchange impairment, and obstructive lung disease. The disease process can become so severe that the only treatment may be lung transplantation.[29]

The most common and major components of e-liquids are propylene glycol or 1,2-propanediol and glycerol or glycerin (propane-1,2,3-triol). Both types of compounds act as solvents for nicotine and flavoring compounds.[4] These compounds are generally well tolerated as food additives and are classified by the US Food and Drug Administration as "generally recognized as safe."[30] However, when inhaled, these solvents have been shown to adversely affect pulmonary tissues.[31] During the generation of vaping aerosols, propylene glycol and glycerin are heated and subsequently form aldehydes as byproducts. When inhaled, these aldehydes are known to induce coughing, asthma exacerbations, and alterations in pulmonary function test results that mimic those of obstructive pulmonary disease, like a decreased forced expiratory volume in the first one second to the forced vital capacity of the lungs (FEV_1/FVC) ratio.[32]

In e-liquids that contain tetrahydrocannabinol (THC), vitamin E is used as a thickening agent to permit vaping of the THC.[33] The inhalation of vitamin E has been found to cause lung surfactant to lose its ability to maintain the surface tension that is necessary to facilitate pulmonary gas exchange.[34] Additionally, when vitamin E is heated to generate aerosols, it creates ketene gas. This gas is highly toxic to pulmonary tissues and has been linked to e-cigarette or vaping use-associated lung injury.[35]

Pulmonary homeostasis is maintained by a multitude of physiological mechanisms including lung surfactants, mucociliary clearance, and phagocytosis of inhaled particulates. Alveolar macrophages are the primary cell line responsible for protecting pulmonary tissues from further injury after they have received an insult. Whether tissue damage is of infectious or inflammatory origin, alveolar macrophages respond to reduce inflammation and limit the extent of injury. Alveolar macrophages are effectors of resolution of inflammation through phagocytosis of apoptotic cells (efferocytosis), preventing dying cells from releasing pro-inflammatory and toxic contents into the environment while triggering the release of anti-inflammatory and repair factors.[36] Exposure to vaping aerosols has been found to change the phenotype and function of alveolar macrophages, suppressing their efferocytotic activity leading to impaired resolution of pulmonary epithelial inflammation.[37] Inhalation of electronic cigarette aerosols also suppresses host response to viral infections. With or without nicotine, these aerosols have been shown to inhibit expression of SPLUNC1 (short palate, lung, and nasal epithelial clone 1), a molecule required for host defense against human rhinovirus.[38]

When e-liquids are heated to generate aerosols, the fine particulate matter byproduct produced creates a pro-inflammatory state within bronchial and alveolar cell lines. This pro-inflammatory state has been linked to the increased generation of reactive oxygen species in response to e-cigarette aerosol inhalation. The generation of reactive oxygen species secondary to electronic cigarette aerosols is capable of triggering apoptosis and programmed necrosis in pulmonary cell lines.[39] Compared with conventional cigarette smoke produced via combustion, vaping aerosols do not produce carbon monoxide. Thus, the use of electronic cigarettes is not associated with an increase in carboxyhemoglobin levels.[40]

Aerosols from electronic cigarette devices affect multiple respiratory system functions including altering airflow, increasing oxidative stress, and interfering with lung development.[32] A recent animal model demonstrated long-term exposure (daily 1-hour exposure for 4

months) to nicotine-containing vapor induced COPD-like features in mice lungs. These findings included increased airway hyper-reactivity, distal airspace enlargement, mucin production, and cytokine and protease expression.[41] Electronic cigarettes have also been linked to suppression of the protective cough reflex. Research has shown that in a group of healthy adult nonsmokers, a single exposure to electronic cigarette aerosols, approximating the nicotine delivery of 1 tobacco cigarette, significantly inhibits cough reflex sensitivity.[42] Therefore, it is not without reason for a sedation/anesthesia provider to consider treating patients who endorse any electronic cigarette use with the same management principles as a COPD or reactive airway patient.

Drug-to-Drug Effects

Patients who regularly use vaping devices are potentially at risk for metabolic interactions between compounds found in electronic cigarette aerosols and anesthetic agents. Electronic cigarettes have been shown to produce volatile organic compounds, including toluene, in every sample of aerosol detected in a study conducted by Zhang et al.[43] Evidence has shown that toluene shares the same effect as many central nervous system (CNS) depressant agents like opioids and barbiturates.

Many patients seeking dental treatment require and/or desire sedative agents when having dental procedures due to dental anxiety or pain. In addition to enjoying the taste of e-liquids, many users endorse consumption of e-liquids with nicotine for its anxiolytic effects. The acute consumption of nicotine has been shown to have anxiolytic properties by altering neurotransmitter secretion within the CNS.[44] It is not without reason to anticipate a patient who uses electronic cigarettes and has dental anxiety to utilize their device prior to sedation or general anesthesia. Consumption of nicotine has also been linked to analgesic and antinociceptive effects that are caused by nicotine interacting with endogenous opioid pathways and binding to central and peripheral nicotine acetylcholine receptors.[45] Subsequently, chronic nicotine use has been associated with patients having an increased opioid requirement postoperatively. A proposed mechanism for the increased opioid requirement postoperatively is alteration in pain thresholds secondary to nicotine abstinence in the preoperative period combined with a receptor-mediated tolerance that develops from chronic nicotine use.[46] In a study conducted by Chiang et al,[47] abstinence for 1 day in nicotine-dependent patients resulted in hyperalgesia and lowered pain thresholds after surgical procedures.

Furthermore, volatile organic compounds and nicotine have been shown to exert CNS depressive effects similar to many sedative agents. Prior to performing a procedure under sedation, the provider should be mindful of these interactions and take a thorough history during their preoperative assessment. In patients who endorse using electronic cigarettes, the sedation and anesthesia provider should inquire about the frequency of use, when the patient last used their device, and what substances they inhale using their device. It is important for the provider to make the distinction between patients inhaling substances other than nicotine (ie, THC products), as patients who vape THC products are at potentially higher risk for perioperative lung injury.[48]

SURGICAL CONSIDERATIONS

Wound Healing

It has been well documented that smoking conventional cigarettes in the perioperative period negatively impacts surgical outcomes. In soft tissue procedures, nicotine has been found to increase the risk of skin flap necrosis and surgical site infection.[49] An animal study found that rats exposed to vaping aerosols have the same rates of skin flap necrosis as those exposed to traditional cigarettes and significantly higher rates of skin flap necrosis compared with a control group.[50] For many years, cigarette smoke has been known to cause local tissue ischemia from combustion-produced carbon monoxide-induced vasoconstriction. In a study conducted by Page et al,[51] which used a thermal imaging camera, a reduction in cutaneous blood flow to the hands and upper extremities was observed in participants less than 10 minutes after inhalation of electronic cigarette aerosols. A reduction in blood flow to a surgical site secondary to aerosol inhalation increases the length of the tissue repair process by prolonging the 4 phases of healing (coagulation/hemostasis; inflammation; proliferation; and wound remodeling).[52]

Nicotine can impair the wound healing process in the oral cavity, has been shown to have antiproliferative properties, and affects gingival fibroblasts in vitro. Gingival fibroblasts actively participate in the tissue repair process by proliferating, migrating, and filling the wound beyond the synthesis of growth factors and extracellular matrix molecules.[53] When gingival fibroblasts are exposed to vaping aerosols, cell migration and wound healing are delayed.[54] Electronic cigarette devices containing nicotine can affect oral myofibroblast differentiation, leading to decreased wound contraction, which also impairs the healing process.[55]

DISCUSSION

Vaping devices remain largely unregulated and are inexpensive to manufacture. Pair this with the widely held misconception that these devices are less dangerous than conventional cigarettes and it is unlikely that there will be a decline in the number of electronic cigarette users for the foreseeable future. Use of vaping devices poses an equal, if not arguably greater threat to one's systemic and oral health than conventional cigarettes. Just like conventional cigarettes, electronic cigarette devices have been linked to the development of a litany of diseases, including but not limited to hypertension, atherosclerosis, asthma, emphysema, and oropharyngeal carcinoma. The use of vaping devices is becoming a public health crisis that is depleting valuable medical resources. Therefore, it is the responsibility of clinicians and anesthesia providers alike to educate the public regarding the true dangers associated with using these devices.

The growing number of electronic cigarette users has serious implications for providers of moderate and deep sedation and general anesthesia in the outpatient dental setting. Sedation and general anesthesia providers should be aware of the acute and chronic systemic effects of electronic cigarette device use to aid in preventing, identifying, and managing adverse events that can occur perioperatively. The adverse event providers will most commonly encounter and that is of greatest concern is airway obstruction. Electronic cigarette devices have been proven to increase airway reactivity and have been linked to the development of asthma in chronic users.[56]

Furthermore, patients with reversible and irreversible obstructive lung disease are at an increased risk of perioperative pulmonary complications. Due to the potential risks associated with the administration of anesthetic agents in all patient populations, the preoperative consultation period is critical to determine if a patient is a suitable candidate for sedation in the office setting. There are 3 key factors to take into consideration when evaluating a patient with a suspected reactive airway for an office-based sedation or general anesthesia: (1) Identify risk factors contributing to a reactive airway or obstructive/restrictive disease; (2) If present, evaluate the severity of diminished lung function; (3) Determine whether the patient's condition can be improved or further optimized prior to the procedure. Assessing these 3 factors will aid in deciding the appropriate anesthetic plan and venue for care (office-based versus hospital-based).

Commonly encountered reactive airway risk factors include active smoking history or electronic cigarette use, active upper respiratory infection, symptomatic poorly controlled asthma, and COPD requiring supplemental oxygen. Patients with positive risk factors should have their pulmonary function tested in the preoperative period to assess severity of their disease. Peak expiratory flow rate (PEFR) and spirometry are 2 commonly used methods to assess pulmonary function. PEFR can be measured in an outpatient setting with a handheld peak flow meter. A PEFR $>80\%$ of predicted indicates the patient's pulmonary function is stable and/or well controlled. In the patient with a repeated PEFR $\leq 80\%$ of predicted, further evaluation should be performed with spirometry.

In patients who admit to or with whom there is warranted suspicion of electronic cigarette use, careful attention should be paid to the respiratory component of the primary survey. This includes monitoring the patient's respiratory effort at rest, examining their airway, and auscultation of breath sounds. Patients who are chronic electronic cigarette device users will likely show physical exam findings similar to asthmatic patients, including wheezing and rhonchi. In asthmatic patients, spirometry can be used in the office setting to evaluate if the patient's asthma is well controlled. An $FEV_1 > 80\%$ of predicted indicates the asthmatic is well controlled. In any patients with repeated $FEV_1 < 80\%$ of predicted, the sedation or anesthesia provider should consider having the patient's pulmonary function optimized prior to the procedure, regardless of whether there is a documented history of asthma.

When evaluating a patient for office-based sedation, a crucial vital sign that should be obtained during the preoperative period in patients who endorse e-cigarette use is room-air oxygen saturation (SpO_2) at rest. In the office setting, a patient's SpO_2 can be obtained inexpensively and in real time using a finger pulse oximeter. The importance of obtaining a baseline SpO_2 in all patients being evaluated for office-based sedation is highlighted by data that show patients with a $SpO_2 < 92\%$, excluding any other conditions, are at a higher risk for perioperative and postoperative pulmonary complications.[57]

Of note, although not commonly used to evaluate the stability of a patient's pulmonary function, chest radiographs can be used as an adjuvant to rule out any lower respiratory tract infection prior to the date of the procedure. In patients with an active respiratory tract infection, elective surgery should be postponed until the patient has been asymptomatic for a minimum of 2 weeks or ideally up to 6 weeks.[50,58] An active respiratory tract infection can increase the risk of perioperative respiratory complications by a multiple of 7.[59]

When treating chronic electronic cigarette users showing signs of reversible obstructive lung disease, it

Recommended Protocol for Optimization of Electronic Cigarette Users

Recommended protocol for optimization of electronic cigarette users
• Use in-office spirometry to assess the presence or severity of any electronic cigarette-related obstructive lung disease
• In patients with mild to moderate obstructive lung disease: ○ Premedicate 20–25 min before procedure start with an inhaled β-2 adrenergic agonist
• In patients with moderate to severe obstructive lung disease: ○ Prescribe PO prednisone 40 mg QD for 5 d + premedicate with a β-2 agonist prior to procedure start in consultation with an appropriate pulmonary specialist
• In high-risk patients, consider a preoperative chest radiograph to rule out any active airway infection
• In patients with a room-air oxygen saturation <92% at rest, refer to primary care physician for further workup and preoperative evaluation prior to proceeding with elective procedures with sedation
• Consider premedication with dexmedetomidine or a suitable benzodiazepine for anxiolysis to reduce catecholamine induced airway reactivity
• Ideally, encourage patients to abstain from using their device for at least 6 wk prior to elective procedures ○ In poorly compliant patients, a preoperative abstinence period of 10 h minimum should be strongly encouraged

is the belief of the authors of this paper that the patient will benefit from having their lung function and airway optimized with the administration of appropriate medications in the days leading up to the procedure as well as during the immediate preoperative period. The authors of this paper recommend prescribing a short course of oral prednisone (40 mg 1 tab PO QD for 5 days) prior to the day of the sedation (Table). In patients with a history of a reactive airway or reversible obstructive lung disease, administration of oral corticosteroids in the preoperative period has been linked to a decreased incidence of peri- and postoperative bronchospasm, as well as decreased oral airway edema and upper airway reactivity.[60]

Continuing, the authors recommend on the day of the sedation during the immediate preoperative period to administer a prophylactic dose of a suitable short-acting β-adrenergic agonist such as albuterol. The prophylactic albuterol can be administered as 2 to 4 puffs from a multidose inhaler just prior to the procedure start or in nebulized form (albuterol 2.5 mg) 20 to 30 minutes prior to any airway manipulations (Table).[61] Administration of an appropriate short-acting β-adrenergic agonist just prior to the procedure start facilitates relaxation of bronchial smooth muscle and increases the mucociliary clearance of sputum, leading to improved perioperative pulmonary function.[62]

In addition to preoperative optimization, the provider can further reduce the probability of experiencing an adverse airway event by adequately premedicating the patient. An optimal premedication decreases patient anxiety and improves work of breathing, while eschewing oversedation and respiratory depression. Although there may currently be no single ideal drug for the purposes of premedication, the authors recommend using dexmedetomidine, an α-2 adrenergic receptor agonist, due to its favorable pharmacological profile. Administration of dexmedetomidine provides anxiolytic, sympatholytic, and antisialagogue effects without causing respiratory depression.[63] Dexmedetomidine can be administered via multiple different routes including intravenous (IV), intramuscular (IM), intranasal, and buccal infiltration. For the purposes of premedication, the authors recommend IV or IM administration. The IV premedication dosage is 0.33–0.67 μg/kg, while the IM premedication dosage is 2.5 μg/kg, either route should be administered 15 minutes prior to procedure start.[64]

Furthermore, in patients with a difficult airway or who have diminished respiratory functionality, the provider can further reduce the incidence of possible airway obstruction via the anesthetic agents they opt to use perioperatively. The authors of this paper recommend ketamine as one of the agents used in a balanced sedation technique. Ketamine is a phencyclidine derivative that acts as an N-methyl-D-aspartate (NMDA) receptor antagonist to cause its anesthetic effects. Ketamine is an ideal agent in a patient with a potentially reactive airway because it allows maintenance of protective airway reflexes while sedating the patient without causing respiratory depression.[65] Using a balanced technique, ketamine should be dosed at 0.5 mg/kg and administered intravenously in small boluses similar to propofol. Ketamine has an onset of 20 to 30 seconds and a duration of 20 to 30 minutes.[66] When used in patients with reactive airways, ketamine should not be administered alone due to increased salivation. The authors recommend administering ketamine with a suitable antisialagogue (eg, glycopyrrolate or atropine) to attenuate the excessive salivation that can occur with ketamine.

Next, acute and chronic electronic cigarette device use has detrimental consequences on the cardiovascular system and centers around nicotine, which causes sympathetic discharge in the autonomic ganglia and adrenal medulla, leading to the release of catecholamines.[67] Patients who vape prior to the administration of sedative or anesthetic agents may present with an elevated heart rate, increased systolic blood pressure, and increased cardiac output. Performing a 12-lead electrocardiogram in the preoperative period can aid in

evaluating patients with high clinical suspicion for right ventricular hypertrophy, potential conduction disturbances, and to rule out evidence of ischemic heart disease.[57] Patients with no history of cardiovascular disease may be able to tolerate nicotine and vaping-associated cardiovascular system changes. For example, the teenager presenting for impacted third molar extractions while tachycardic is unlikely to be at major risk for an acute coronary syndrome. However, the middle-aged patient with some underlying pre-existing medical comorbidities (eg, hypertension or atherosclerosis) may not be able to tolerate these baseline changes, and therefore, perioperative cardiovascular changes in this type of patient may have the potential to significantly increase morbidity during the perioperative administration of sedative and anesthetic agents. Taking this into consideration, the serum half-life of nicotine is ~2 hours.[19] The authors recommend educating the patient and encouraging them to withhold from electronic cigarette device use for at least 10 hours prior to the administration of any sedative or anesthetic agents in order to reduce acute cardiovascular changes perioperatively.

Additionally, the nicotine in cigarette smoke has been found to induce hepatic microsomal enzymes and enhance the activity of cytochrome P-450 mixed oxidase metabolic pathway. Subsequently, nicotine consumption profoundly alters pharmacodynamics and pharmacokinetics of many anesthetic agents undergoing hepatic metabolism. Currently, it is recommended that a smoker abstain for a period of 6 weeks prior to elective surgery in order to allow hepatic enzymes and the immune system to return to baseline levels, thus making drug metabolism more predictable.[67] The nicotine content found in vaping aerosols can be 2–3 times that of cigarette smoke depending on the construction of the device and the nicotine concentration within the e-liquid.[68] Therefore, the authors recommend an abstinence period of 6 weeks minimum for electronic cigarette device users undergoing elective procedures.

The use of electronic cigarette devices has been linked to decreased wound healing capabilities and increased postoperative surgical complications. In cigarette smokers who are planning to undergo surgery, it is recommended that cessation begin 6 to 8 weeks prior to surgery.[69] There are currently no recommendations for when an electronic cigarette user should initiate cessation to improve surgical outcomes. Nevertheless, given how electronic cigarette use causes comparable end-organ effects to conventional cigarettes, it is the author's belief that electronic cigarette users should be treated like cigarette smokers, and a 6- to 8-week cessation period be recommended to patients undergoing dental sedation.

CONCLUSION

Consumption of electronic cigarettes is not free of consequences to one's systemic and oral health. Peer reviewed literature now supports that the aerosols generated by e-cigarettes have detrimental effects on the health of multiple organ systems including the cardiovascular, pulmonary, and CNSs. Even with emerging literature illustrating the harmful effects of e-cigarettes, these devices remain largely unregulated, and given the current statistical trends, the number of e-cigarette users seeking dental care will continue to rise. Providers of sedation and general anesthesia for dentistry must anticipate an increasing number of patients being e-cigarette users. Similar to patients who smoke tobacco, the modern anesthesia provider must be knowledgeable about the systemic effects of e-cigarette aerosols in order to optimize patient care throughout the perioperative period.

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CONTINUING EDUCATION QUESTIONS

This continuing education (CE) program is designed for dentists who desire to advance their understanding of pain and anxiety control in clinical practice. After reading the designated article, the participant should be able to evaluate and utilize the information appropriately in providing patient care.

The American Dental Society of Anesthesiology (ADSA) is accredited by the American Dental Association and Academy of General Dentistry to sponsor CE for dentists and will award CE credit for each article completed. You must answer 3 of the 4 questions correctly to receive credit.

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CE questions must be completed within 3 months and prior to the next issue.

1) Electronic cigarette use increases platelet aggregation as quickly as _____ after exposure to vaping aerosols.

a. 1 minute
b. 15 minutes
c. 2 hours
d. 7 days

2) "Popcorn lung" is a condition affecting the pulmonary system characterized by:

a. areas of micro-pneumothorax located at the base of the lung.
b. audible crackles upon expiration when lung fields are auscultated.
c. proliferation of granulation tissue in bronchiolar epithelium.
d. radiopaque lesions the shape of popcorn kernels on chest radiographs.

3) Which of the following are sequelae from e-cigarette use?

a. Increased airway hyper-reactivity
b. Increased mucin production
c. Increased production of tumor necrosis factor-α (TNF-α)
d. All of the above

4) According to the authors, which of the following conditions places patients at higher risk in developing perioperative pulmonary complications?

a. Patient abstains from e-cigarettes for >6 weeks.
b. Patient has a forced expiratory volume in the first one second (FEV_1) of > 80%.
c. Patient has baseline oxygen saturation <92%.
d. Patient is treatment planned for placement of >4 implants.

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

Baxter M, Mincer J. Cognitive recovery by decade in healthy 40- to 80-year-old volunteers after anesthesia without surgery. Anesth Analg. 2022;134(2):389-399. doi:10.1213/ANE.0000000000005824

Postoperative delirium and postoperative cognitive dysfunction are the most common complications for older surgical patients. General anesthesia may contribute to the development of these conditions, but there are little data on the association between age and cognitive recovery from anesthesia in the absence of surgery or underlying medical condition. This single-center cohort study examined the postanesthetic cognitive function in healthy adult volunteers, age 40 to 80 years (N = 71, mean age 58.5 years, 44% women) with no underlying cognitive dysfunction. Volunteers underwent cognitive testing before and at multiple time points after 2 hours of general anesthesia consisting of propofol induction and sevoflurane maintenance, akin to a general anesthetic for a surgical procedure, although no procedure was performed. The primary outcome was time to recovery to cognitive baseline on the Postoperative Quality of Recovery Scale (PQRS) within 30 days of anesthesia. Secondary cognitive outcomes were time to recovery on in-depth neuropsychological batteries, including the National Institutes of Health Toolbox and well-validated paper-and-pencil tests. The primary hypothesis was that the time to recovery of cognitive function after general anesthesia would increase across decades from 40 to 80 years of age. This was examined with discrete-time logit regression (for the primary outcome) and linear mixed models for interactions of age decade with time postanesthesia (for secondary outcomes). No association was found between age group and recovery to baseline on the PQRS: 52% of volunteers recovered within 60 minutes after anesthesia, and 91% recovered by day 1. Hazard ratios (95% confidence interval) for each decade compared with 40- to 49-year-olds were 50 to 59 years, 1.41 (0.50-4.03); 60 to 69 years, 1.03 (0.35-3.00); and 70 to 80 years, 0.69 (0.25-1.88). There were no significant differences between older decades relative to the 40- to 49-year reference decade in recovery to baseline on secondary cognitive measures. The authors concluded that recovery of cognitive function to baseline was rapid and did not differ between the age decades of participants, although the number of individuals in each decade was small. These results suggest that anesthesia alone may not be associated with cognitive recovery in healthy adults of any age decade.

Anesth Prog 69:53–55 2022

Erlich C, Lamer A, Moussa M, Martin J, Julien R, Rogeau S, Tavernier B. End-tidal carbon dioxide for diagnosing anaphylaxis in patients with severe postinduction hypotension. Anesthesiology. 2022;136(3):472-481. doi:10.1097/ALN.0000000000004123

Perioperative hypersensitivity reactions may be difficult to diagnose during general anesthesia. Postinduction hypotension is the most common sign but is not specific. In this retrospective, single-center case-control study, the authors compared $EtCO_2$ in patients with a diagnosis of anaphylaxis and in patients with severe hypotension from any other cause after the induction of anesthesia. The anaphylaxis group was formed based on tryptase/histamine assay data and allergy workup data recorded over the period of 2010 to 2018. The control (hypotension) group consisted of all patients having experienced severe hypotension (mean arterial pressure <50 mmHg for 5 minutes or longer) with a cause other than anaphylaxis after anesthesia induction in 2017. The anaphylaxis and hypotension groups comprised 49 patients and 555 patients, respectively. The minimum $EtCO_2$ value was significantly lower in the anaphylaxis group than in the hypotension group. The area under the receiver-operating characteristic curve (95% confidence interval [CI]) for $EtCO_2$ was 0.95 (0.91-0.99). The sensitivity and specificity (95% CI) for the optimal cutoff value were 0.92 (0.82-0.98) and 0.94 (0.92-0.99), respectively. In the multivariable analysis, the minimum $EtCO_2$ was associated with anaphylaxis after adjusting for confounders and competing predictors, including arterial pressure, heart rate, and peak airway pressure. The authors concluded that low $EtCO_2$ was a sensitive, specific, independent marker of anaphylaxis in mechanically ventilated patients with severe postinduction hypotension.

Comment: The authors found anesthetic overdose to be the most common cause of severe postinduction hypotension. They also note that while reduced $EtCO_2$ was associated with anaphylaxis in this study, bronchospasm also alters expired CO_2. Anaphylaxis may begin very early during induction, with signs being confounded by induction drug overdose and potential bronchospasm. The main limitation of the study was the retrospective, single-center design.

Larach D, Hah J, Brummett C. Perioperative opioids, the opioid crisis, and the anesthesiologist. Anesthesiology. 2022;136(4):594-608. doi:10.1097/ALN.0000000000004109

This focused review covers the major components of perioperative anesthesia care, including identification of the patient at risk for prolonged opioid use or misuse, expectations for postoperative pain control, postoperative opioid tapering and cessation, intraoperative opioid administration, managing the patient with an opioid use disorder, and surgeon prescribing practices.

Comment: Perioperative opioid management remains complex, as the number of prescription-related opioid deaths continues to rise.[1] The authors acknowledge the suggestion that "opioid-free" anesthesia become the standard of care but note a weak underlying rationale and lack of evidence for this suggestion. At the time of this review, the authors found no evidence that the total avoidance of opioids during anesthesia improves outcomes other than postoperative nausea and vomiting.

Nolan JP, Ornato JP, Parr MJA, Perkins GD, Soar J. Resuscitation highlights in 2021. Resuscitation. 2022;172:64-73. doi:10.1016/resuscitation. 2022.01.015

This article is a summary of the key papers published in the journal *Resuscitation* in 2021. Ninety-eight papers are briefly summarized and described by the editorial staff. General categories of topics include epidemiology, basic life support, advanced life support, pediatric and neonatal resuscitation, trauma, and postresuscitation care. Included are the 2021 Guidelines for Resuscitation of Cardiac Arrest in Special Circumstances from the European Resuscitation Council (ERC), which includes a special section on dental offices.

Comment: The ERC acknowledges the limited space in dental operatories and the need to perform chest compressions in a dental chair as significant challenges to resuscitation. The last set of guidelines, published in 2015, explicitly recommended performing cardiopulmonary resuscitation on patients while they were reclined in a dental chair, using a stool to stabilize the back of the chair during chest compressions. The 2021 guidelines note limited in vitro evidence to support this recommendation. The use of the intraosseous (IO) route continues to be recommended in Pediatric Advanced Life Support (PALS) guidelines when intravenous (IV) access cannot be maintained; however, the article cites 3 studies that fail to show a clear benefit with IO access, prompting a call for randomized trials to compare IV and IO access in the setting of PALS.

Porter S, Renew J. Development, validation, and results of a survey of personal electronic device use among 299 anesthesia providers from a single institution. Anesth Analg. 2022;134(2):269-275. doi:10.1213/ANE. 0000000000005708

The pattern of perioperative use of personal electronic devices (PEDs) among anesthesia providers in the United States is unknown. The authors of this article developed a 31-question anonymous survey of perioperative PED use that was sent to 813 anesthesiologists, anesthesiology residents, and certified registered nurse anesthetists at 3 sites within 1 health system. The electronic survey assessed patterns of PED use inside the operating room (OR), outside the OR, and observations of peers. Questions were designed to explore the various purposes for PED use, the potential impact of specific hospital policies or awareness of medicolegal risk on PED use, and whether PEDs were a source of perioperative distraction. The overall survey response rate was 36.8% (n = 299). Twenty-four percent of respondents reported texting inside of the OR, 5% reported talking on the phone, and 11% reported browsing on the internet. When outside of the OR, 88% reported texting, 26% reported talking on the phone, and 63% reported browsing the internet. Two percent of respondents self-reported a distraction from clinical care while in the OR, compared with 15% who had observed a distraction in others. Eighty percent of respondents recognized PED as a potential distraction for patient safety. The authors conclude PED use is prevalent among anesthesia providers.

Comment: PEDs in this survey included cell phones, tablets, and other portable devices. An accompanying editorial to this article acknowledges the ubiquity of cell phone usage alone, noting the number of cell phones alone has outnumbered the world's population since 2019. Strategies are discussed for using PEDs while maintaining vigilance during patient care.

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