REVIEW PAPER

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Abstract
Clinical monitoring and technology are at the heart of anesthesiology, and new technological developments will help to define how anesthesiology will evolve as a profession. Anesthesia related research published in the JCMC in 2018 mainly pertained to ICU sedation with inhaled agents, anesthesia workstation technology, and monitoring of different aspects of depth of anesthesia.

Keywords Anesthesia · Depth of anesthesia · Anesthesia equipment · Airway · Neurophysiologic monitoring

1 ICU sedation with inhaled agents

Several technological innovations have facilitated delivery of inhaled agents to sedate mechanically ventilated ICU patients. A special issue of the Journal of Clinical Monitoring and Computing contained several manuscripts describing these new technologies. An accompanying editorial summarized the published work well, and several aspects are reiterated in this review [1].

Why bother with the delivery of inhaled agents in the ICU? First, the partial pressure of inhaled agents can be measured continuously in the inspired and expired gas, allowing precise titration and early detection of any potential device failure [2]. Second, data suggest patient outcome may be improved when inhaled agents rather than intravenous sedatives are used [3]. Three, inhaled agents have an enormous safety record when used intraoperatively (barred extremely rare cases of malignant hyperthermia or hepatotoxicity). Their effects after long(er) term use in the ICU remain less well studied, but the review by Manatpon and Kofke [4] is reassuring. Finally, ICU contamination by trace gases, its management, and its clinical significance was reviewed [5].

Vaporization of liquid agent needs to be well controlled [2] because the partial pressures they generate if uncontrolled (i.e. the vapor pressure at the prevailing room temperature) are lethal. While anesthesia machines accomplish this by the use of vaporizers or liquid injectors, the most widely published on delivery tools in the ICU are the AnaConDa (Sedana Medical, Uppsala, Sweden) and the Mirus (Medcaptain Medical Technology, Shenzhen, China). Their mechanism of action was reviewed by Farell et al. and Bomberg et al., respectively [6, 7]. The devices deliver the inhaled agent at the Y-piece, which is the connection between the in- and expired breathing hoses of the ventilator and the endotracheal tube of the patient. Waste is minimized by reflecting part of the exhaled agent back during the next inspiration using a charcoal filter [6–9]; some loss is obligatory to allow the partial pressure to be decreased at a sufficiently rapid rate. This waste is equivalent to that used by an anesthesia machine with a fresh gas flow of 1 L/min, but the absolute amount wasted into the atmosphere is lower because the partial pressures for sedation are lower than those for general anesthesia. This wasted gas has to be scavenged, and the methods to do so have were described by [5]. Isoflurane and sevoflurane seem to be the most frequently used agents, but desflurane can also be used [8]. The Mirus system reliably delivers 1.0 MAC of the modern inhaled agents, but this may not suffice to prove a sufficient surgical depth of anesthesia in all patients [10].

Any device added at the patient–machine interface adds resistance and/or dead space, which will increase the work of

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breathing. This has been explored [11–13], and will deserve particular attention in children. Reducing the size of the device does reduce the work of breathing [13].

The group by Fisher et al. described a novel approach, the RIVAL, where the reflective device is replaced by a vaporizer controlling the inspired concentration into a second circle system proximal of the Y-piece [14]. Another unexplored yet intriguing approach would be to use an anesthesia machine that has the ventilator modes offered by an ICU ventilator yet allows rebreathing of inhaled agents.

The accompanying editorial concludes that "inhaled anesthetic agent sedation in the ICU is coming of age, and the special issue addresses the delivery tools, the potential benefits and drawbacks, and appropriate scavenging techniques" [1].

2 Anesthesia workstation technology

The number of manuscripts submitted to the journal that address anesthesia work station technology remains extremely low. This is worrisome because "workstation technology is advancing at a very rapid pace, and proper understanding of the underlying technology and willingness to stay ahead of new technological developments is key to the preservation of the profession of anesthesiology—failing to do so leads to the anesthesia provider becoming "a" or "the" major factor impeding introduction of these new technologies. If not, patients will be wondering why they flew in for surgery on a pilot free Boeing and self-driving car to find themselves being cared for by an anesthesia provider still setting the fresh gas flows and vaporizer settings" [15]. The journal wants to repeat its plea and encourage researchers to submit work related to the anesthesia workstation technology.

Hendrickx et al. continue to dissect out the details of how automated low flow delivery systems manage fresh gas and agent control, and how the use of low flows affects agent and CO_2 absorbent use. The amount of desflurane usage with the FLOW-i anesthesia machine in automatic gas control is described, which provides a quantative basis for discussions about cost and pollution [16]. The use of N_2O reduced the use of desflurane proportional to the MAC reduction by N_2O. The rate of rise of the end-expired desflurane and N_2O with three different wash-in speeds are described, a feature that may serve to minimize both under dosing (rendering the patient prone to awareness) and overdosing (rendering the patient prone to hypotension).

A reduction of fresh gas flows will also increase CO_2 absorbent use because more rebreathing will cause more CO_2 to pass through the absorbent. Many factors affect the performance of a particular CO_2 absorbent, such as chemical composition (mainly NaOH content), shape of the granules,

shape and volume of the canister holding the product, and the type of anesthesia machine. The most recent publication describes the in vitro performance of prefilled CO_2 absorbers with the Zeus® [17]. An accompanying editorial by Jeffrey Feldman examines whether it matter which CO_2 absorbent one uses [18].

3 Monitoring of different aspects of depth of anesthesia

Several studies examine a wide range of topics related to depth of anesthesia.

Changes in concentrations of oxygenated and deoxygenated hemoglobin as well as in blood volume measured with near infrared spectroscopy (fNIRS) were found to be associated with the transition between maintenance and emergence that occurs as a result of sevoflurane washout and carry information that allows real time and automatic classification of the anesthetized state with high accuracy [19]. Whether this suffices to translate fNIRS into a clinically useful parameter of depth remains speculative.

Intraoperative lidocaine infusion is used as an adjunct to general anesthetics. When a volatile anesthetic agent and fentanyl were titrated to maintain hemodynamic stability, the addition of lidocaine lowers the MAC required to maintain hemodynamic stability but BIS values were higher [20]. The authors entertain the idea that "BIS may not be a sensitive indicator of synergistic interactions between local anesthetic and volatile agent" and "advocate a cautious approach to titration of general anesthesia when combined with lidocaine infusion". It is unfortunate that lidocaine in this study was titrated to maintain hemodynamic stability, which is known to be a notorious poor and unreliable indicator of depth of anesthesia.

Existing electroencephalography (EEG) based depth of anesthesia monitors cannot reliably track sedative or anesthetic effects induced by ketamine, xenon, and N_2O, all NMDA receptor antagonists. The so-called brain anesthesia response (BAR) monitor uses a "physiologically-motivated depth of anesthesia monitoring" algorithm that is based on fixed-order ARMA (autoregressive-moving-average) modeling [21]. Its parameters cortical state (CS), cortical input (CI), composite cortical state (CCS), and especially composite cortical state distance (CCSd) are able to differentiate gas concentration and responsiveness levels in people receiving N_2O. Their utility in the clinical environment needs to be proven.

The BIS monitor was used as a tool to measure postoperative sleep status in the first night after thyroidectomy after propofol or sevoflurane anesthesia [22]. Four outcome measures were examined: duration of sleep, sleep efficiency index (SEI), area under the curve (AUC) of the BIS value over

time, and stage N3 sleep. Sleep was defined as a BIS below 80, stage N3 sleep as BIS < 55, duration of sleep as the total time spent with BIS < 80, and SEI as the ratio of a patient's total sleep time over the time available for "nocturnal" sleep (12 h). BIS-AUC was calculated by using the trapezoidal rule. Compared to sevoflurane anesthesia, propofol anesthesia decreases the BIS-area under the curve, increased the sleep efficiency index, and increased the durations of postoperative sleep and sleep stage N3 by 110.5 and 36.5 min per patient. This prompted the authors to conclude propofol might improve sleep time immediately after thyroidectomy.

Ultimately, it is hoped that monitoring alters intermediate and clinically meaningful outcome parameters. The combined use of entropy and surgical pleth index monitoring was shown to reduce the incidence of hypotension and fentanyl and vasopressor during surgery in critically ill polytrauma patients [23].

Depth of sedation in the ICU patient is often monitored by behavioral responses; the most widely used is the Richmond Agitation Sedation Scale (RASS) [24]. In a study with a small number of patients, the desired level of sedation was achieved in only 40% of patients during propofol administration. Inadequacy of sedation was further documented by the NeuroSENSE™ monitor, an EEG-based continuous sedation assessment tool, which according to the authors supports the limitations of the RASS to guide ICU sedation. The authors conclude the potential added benefit of continuous brain monitoring in this setting needs to be explored further.

The pupillary dilation reflex after applying a noxious stimulus is related to the intensity of the stimulus. The reflex can also be used to assess to what extent drugs suppress this response, allowing drug titration - i.e. the reflex can be used to measure "nociception" (if defined as such). While well validated in the presence of propofol and inhaled agents, the pupillary response to nociceptive stimuli has never been studied for ketamine. Ketamine differs from these other drugs because it causes mydriasis and exerts its anesthetic effects via NMDA receptor. The effect of ketamine on the usefulness of the pupillary dilation reflex to measure "nociception was measured 2 min after an intravenous 1 mg kg^{-1} ketamine bolus by tetanic stimulations" [25]. These tetanic stimulations were associated with changes in pupillary diameter and heart rate. The magnitude of changes was significantly influenced by the intensity of stimulation, and movement was associated with a 32% increase in diameter. In children, pupillary reflex dilation to nociceptive stimuli persisted under deep sedation, and its magnitude depends on the intensity of the stimulation. These results again confirm the potential of pupillometry to monitor nociception in anaesthetized subjects, including those receiving ketamine.

Another nociception monitor is the Analgesia Nociception Index (ANI) monitor. The ANI derives the ratio of autonomic sympathic activity vs that of the parasympathic system from heart rate variability. Titration of opioids towards an ANI between 50 and 70 after a thoracic paravertebral block in patients undergoing breast surgery under general anesthesia decreased average remifentanil use by approximately 30%, suggesting that monitoring the ANI detected the suppression of noxious stimuli conferred by the paravertebral block and that the ANI can optimize opioid titration [26]. ANI may also be an objective tool to measure some aspects of the hypnotic state [27].

4 Ensuring the airway

Aspiration is still a risk in dental surgery under general anesthesia with an endotracheal tube (ETT) in situ, especially if a mouth prop is used to facilitate oral exposure. Canpolat et al. [28] studied the effect of a mouth prop on ETT intracuff pressure during dental rehabilitation surgery in children. The mean intracuff pressure before insertion (28.3 ± 2.01 cm H_2O) was increased (P < 0.001) after insertion of the mouth prop (30.8 ± 2.7) and at 30 min (29.6 ± 3.7), indicating the need for strict measurement and readjustment of cuff pressures when used in children during dental rehabilitation surgery.

In 70 patients undergoing elective thoracotomy, the Univent tube (UT) with a bronchial blocker and the EZ-blocker (EZ) with a Y-shaped double-cuffed distal end were found to perform equally well during one-lung ventilation [29]: airway pressures, oxygenation, ventilation and haemodynamics did not differ.

It is a standard recommendation to keep the endotracheal cuff (ETTc) pressure between 20 and 30 cm H_2O. Özcan et al. studied the average ETT cuff pressure before and after a training seminar in 200 patients intubated in the operating theatre [30]. The mean cuff pressure before (54 cm H_2O) and after (33 cm H_2O) the training differed (P < 0.001). Regular training might prevent potential complications related to under-pressured or over-pressured cuffs.

Aleksandrowicz et al. compared the mean pressure exerted on the tongue, the overall endotracheal intubation success rate, and the difference in exerted pressures by four videolaryngoscopes and a Macintosh laryngoscope during simulated conditions (manikin with reduced cervical spine mobility) [31]. The 40 anesthesiologists that performed intubation all had been in practice for at least 15 years, and 18 of them were female. All four videolaryngoscopes resulted in lower mean pressure exerted on the tongue than the Macintosh laryngoscope (P < 0.0001). Failure to intubate the trachea occurred with all devices, with the highest rate (25%) when the Airtraq® was used. Female anesthesiologists exerted lower pressures during intubation than their male colleagues and had higher successful intubation rates.

Wang et al. asked twenty-nine anesthesia residents (10 first-year; 9 s-year; and 10 third-year trainees) to measure one another's thyromental distance (TMD) based on landmark identification of the thyroid cartilage prominence, and then compared these results with MTD measurement by ultrasound [32]. The measurement error rate of the females' TMD was higher than that of the males' (50 vs 10%, P < 0.001). The error rates of anesthesia trainees of the first-year, second-year and third-year were 34, 27, and 31%, respectively (not significantly different).

The majority of studies on safety and efficacy of supraglottic airway devices (SADs) have been done on Caucasian patients. These results may not be extrapolated to Asian patients with different airway anatomy. Therefore, Chaw SH et al. compared the performance of two SADs, i.e. LMA-Supreme with LMA-ProSeal size 1.5 in sixty children (weight 5–10 kg) of Asian descent undergoing general anesthesia during elective surgery [33]. The two devices did not differ with regard to oropharyngeal leak pressure for a size 1.5 (19.1 vs 19.8 cm), first attempt success rate at, fibreoptic grading of the view of the larynx, and airway complications. The patients in whom the insertion failed, were all small (5–6.2 kg). Summarized, both devices maintained an adequate airway without significant complications in a population of Asian children.

5 Neuromonitoring

A retrospective review of 282 neuromonitored shoulder arthroplasty cases was conducted by Aleem et al. [34]. The ipsilateral axillary nerve is the primarily vulnerable neural structure during these procedures. The authors monitored patients' deltoid (all three heads) and other muscles in both arms. The Transcranial Motor Evoked Potential (TcMEP) alert criterion was an 80% decrease in amplitude of TcMEP, not corrected by a 20% increase in stimulus intensity. The authors further noted that alerts not including all three heads were sometimes followed by a decision to proceed despite the alert. Alerts were called in 102 cases (36.1%). When a neuromonitoring alert was given, the major intervention was a pause in surgery to remove retractors and briefly return the operated arm to a neutral position. Neurologic exams were conducted postoperatively and patients were followed for at least 1 year. Motor deficits were defined as 3/5 weakness or worse. A significant reduction in the closing motor evoked potential amplitude, using the 80% threshold alert criterion, was associated with a transient post-operative neural deficit in two cases (0.7%), both in total shoulder arthroplasty, yielding a sensitivity of 100% (95% CI 98.9–100%) and a specificity of 93.9% (95% CI 91.1–96.4%). In a post-hoc analysis of a subset using a stringent criterion (100% decrease of TcMEP amplitude, all 3 deltoid heads), the

sensitivity remained 100% (95% CI 98.0–100%) and the specificity improved to 98.0% (95% CI 95.3–100%). The results of this study suggest that a cohort study of monitored and unmonitored cases may be indicated.

The prone position during spine surgery can be rarely associated with visual loss. Soffin, et al. conducted a prospective pilot study of 20 lumbar spine surgeries to test the visual monitoring capability of a proprietary device, SightSaverTM [35]. Although the observed flash visual evoked potentials proved very sensitive to general anesthetics, the device was safe and reliable potentials could be identified in 36/40 eyes. A future case series should be done to elucidate the best anesthetic protocol for reliable potential recordings and to begin to define alert criteria.

Ushio and colleagues evaluated the facilitating effects of repetitive multi-train transcranial electrical stimulation in neurologically impaired patients undergoing spine surgery [36]. A series of 10 train stimulations were recorded at multi-train rates of 1 and 5 Hz (1000 ms and 200 ms inter-train intervals). In patients with preoperative neurological deficits, the 5 Hz multi-train rate markedly facilitated MEPs of all recorded limb muscles. No minor or major complications of the technique were reported. This technique may be best suited for neurologically impaired patients in whom routine facilitation techniques (double train stimulation, e.g.) is less than optimal.

Somatosensory evoked potentials (SSEPs) are often assessed to estimate prognosis after traumatic brain injury. Decompressive craniectomy may be employed as a life-saving intervention in the setting of severe traumatic brain injury. Because the intact skull manifests the major SSEP voltage/amplitude drop, Bethune, et al. studied SSEP amplitudes in patients before and after craniectomy in brain trauma patients [4]. In bone removed subjects, the SSEP cortical amplitude was approximately doubled compared to pre-operative studies [37]. The authors suggest further longitudinal trials to assess SSEP-mediated neuroprognosis in these patients, taking into account and extending the SSEP data from their pilot study.

Lieberman, et al. studied the difficult problem of TcMEP amplitude reductions, commonly seen when monitoring spine surgery complicated by severe blood loss [38]. The authors employed a hemorrhaged porcine model to define changed cardiac output and propofol level. They hypothesized that blood loss raises propofol levels which may account in part, or in the main, for reduced TcMEP amplitudes in this condition. Blood was removed in six animals to achieve a 60% reduction in TcMEP amplitude. Multivariate analysis revealed the TcMEP change was "primarily associated" with the propofol level increase but was independently related to reduced cardiac output as well. The standard practice to replace volume, correct fallen hemoglobin level, and lower propofol level to reduce cardiodepressant effects is

supported by this data. The authors point out the preference for propofol during neuromonitored spine surgery is complicated by its predictable pharmacokinetics after severe blood loss leading to possible false-positive TcMEP changes.

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