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Monitored anesthesia care in and outside the operating room

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Monitored anesthesia care (MAC) is an anesthesia technique combining local anesthesia with parenteral drugs for sedation and analgesia. The use of MAC is increasing for a variety of diagnostic and therapeutic procedures in and outside of the operating room due to the rapid postoperative recovery with the use of relatively small amounts of sedatives and analgesics compared to general anesthesia. The purposes of MAC are providing patients with safe sedation, comfort, pain control and satisfaction. Preoperative evaluation for patients with MAC is similar to those of general or regional anesthesia in that patients should be comprehensively assessed. Additionally, patient cooperation with comprehension of the procedure is an essential component during MAC. In addition to local anesthesia by operators or anesthesiologists, systemic sedatives and analgesics are administered to provide patients with comfort during procedures performed with MAC. The discretion and judgment of an experienced anesthesiologist are required for the safety and efficacy profiles because the airway of the patients is not secured. The infusion of sedatives and analgesics should be individualized during MAC. Many procedures in and outside of the operating room, including eye surgery, otolaryngologic surgery, cardiovascular procedures, pain procedures, and endoscopy are performed with MAC to increase patient and operator satisfaction.

Key Words: Analgesics, Monitored anesthesia care, Sedatives.

Introduction

The American Society of Anesthesiologists (ASA) defines monitored anesthesia care (MAC) as a planned procedure during which the patient undergoes local anesthesia together with sedation, and analgesia is provided by an anesthesiologist [1]. A responsible anesthesiologist with a broad understanding of drug application performs the MAC since the degree of sedation and analgesia is dependent on the characteristics of the procedures and patients. Sedation during MAC may be considered safer than that of general anesthesia in that less drugs are typically administered. However, the application of sedatives and analgesics should be titrated to avoid central respiratory depression and airway obstruction, since the airway of the patient is not secured during MAC. Preoperative evaluation, perioperative management, monitoring, and postoperative recovery care of MAC is similar to those of general or regional anesthesia. Moreover, the attending anesthesiologist should be aware of the possibility of airway obstruction, desaturation, or even aspiration due to the possibility of deep sedation after infusion of a combination of two or more drugs.

The use of MAC as the technique of choice for a variety of diagnostic and therapeutic procedures in and outside of the operating room is increasing due to rapid postoperative recovery with relatively small amounts of sedatives and analgesics compared to general anesthesia. Additionally, investigations on the effect of MAC on postoperative outcomes have been increasing. Therefore, the responsibility and roles of the anesthesiologist

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should be considered in terms of the safety and effectiveness of MAC. In this review, MAC in and outside of the operating room was described in terms of preoperative patient evaluation, monitoring, and intraoperative care with sedatives and analgesics during a variety of procedures and potentially serious complications.

The Definition and Purpose

According to the ASA, a MAC is a planned procedure during which the patient undergoes local anesthesia together with sedation and analgesia [1]. During MAC, systemic sedation and analgesia is provided by an anesthesiologist, and local anesthesia, including local infiltration or field block, is mainly performed by a surgeon. MAC should be distinguished from simple sedation/analgesia in that sedation/analgesia is performed by a non-anesthesiologist, whereas sedation and analgesia during MAC is provided by an anesthesia care team [2]. Therefore, preoperative evaluation, intraoperative monitoring, and postoperative care for patients with MAC are the same as those with general or regional anesthesia.

The purposes of sedation during a MAC are to provide patients with safe sedation, comfort, pain control, and satisfaction [1]. Safe sedation is achieved due to the wide spectrum of knowledge on sedatives and analgesics available to the attending anesthesiologist; the degree of sedation should be individualized according to the medical condition of the patients. In addition, each diagnostic and therapeutic procedure requires a different degree of sedation and analgesia, and the amount of drug should be carefully titrated. The administration of the proper dosage of anxiolytics as a premedication can provide patient amnesia and comfort without compromising cardiovascular function. Adequate control of pain with analgesia during and after the procedure can contribute to satisfactory MAC, allowing patients to be discharged as quickly as possible [1].

Preoperative Evaluation

Preoperative evaluation of patients with MAC is not different from that of patients given general or regional anesthesia; in all cases, patients should be comprehensively assessed. In addition, patient cooperation is essential during MAC [3]. Patients undergoing MAC are able to respond to orders; therefore, whether they are ready for the procedure should be evaluated. If the patients cannot cooperate, general anesthesia may be a better alternative. On the other hand, there are no specific exclusion criteria for a MAC, and this anesthetic technique can be performed even for the elderly or high perioperative risk patients.

Communication between patients and the anesthesia care team can be used as a tool for monitoring sedation levels and to offer verbal assurance; it can also improve patient cooperation [4]. MAC may be chosen due to patient cardiovascular and respiratory instability, but persistent cough or movement during microscopic procedures may limit the use of MAC. Therefore, preoperative evaluation of whether patients can cooperate without movement during the procedure should be determined.

Preoperative visits are helpful for the patient-anesthesiologist relationship, in that patients can be informed about safe and comfortable analgesia, as well as provided with an explanation regarding the MAC procedure. Communication between patients and anesthesiologists is essential for evaluation of the level of consciousness during infusion of sedative and analgesics for MAC. The patient's physical status, including cardiovascular and respiratory capacity, may determine or affect their sensitivity to sedatives and analgesics. Assessment of co-morbidity, past history, drug reactions, and postoperative anesthetic complications are required during the preoperative visit. The number of ambulatory surgeries performed without allowing sufficient time for preoperative evaluation and patient informed consent has increased recently, although an adequate explanation of anesthesia can be given in preoperative patient clinics.

Intraoperative Monitoring

The ASA has established a basic level of patient monitoring during MAC. Intraoperative monitoring should be effective, applicable, noninvasive, and economical [4]. The presence of a qualified anesthesiologist is essential and patient oxygenation, ventilation, circulation, and temperature must be monitored continuously [4].

Prevention of respiratory depression through continuous respiratory monitoring is essential during the infusion of sedatives and analgesics for MAC. Pulse oximetry is useful for monitoring patient oxygenation, but its use is limited due to the delayed detection of hypoxemia during sedation. Real time detection of hypoxemia with capnography is required immediately, and precordial or esophageal stethoscopes can be used for continuous monitoring of ventilation and inspired oxygen [5]. In addition, the attending anesthesiologist should observe clinical signs continuously through detection of arterial pulses and observation of chest movement and the surgical field.

Monitoring the Level of Consciousness

In addition to standard monitoring, evaluation of the sedation level is of extreme importance during MAC, in terms of the safety and efficacy of the sedatives [4]. For this purpose, clinical or electroencephalographic methods can be used.

For clinical evaluation, several scales pertaining to the sedation level during MAC have been used to reduce the subjectiv-

Table 1. Observer Assessment of Alertness/Sedation Scale (OAA/S) [6]

Level of responsiveness	Speech	Facial expression	Eyes	Score
Responds readily to name spoken in normal tone	Normal	Normal	Clear, No ptosis	5
Lethargic responses to name spoken in normal tone	Mild slowing or thickening	Mild relaxation	Glazed or mild ptosis (less than half the eye)	4
Responds only after name is called loudly and/or repeatedly	Slurring or prominent slowing	Marked relaxation (slack jaw)	Glazed and marked ptosis (half the eye or more)	3
Responds only after mild prodding or shaking	Few recognizable words			2
Does not respond to mild prodding or shaking				1

Table 2. Ramsay Sedation Scale [7]

	Response to command	Score
Awake level	Patient anxious or agitated or both	1
	Patient co-operative, oriented, and tranquil	2
	Patient responds to commands only	3
Asleep level	Brisk response to light glabellar tap	4
	Sluggish response to light glabellar tap	5
	No response	6

ity of anesthesiologist judgments. The Observer Assessment of Alertness/Sedation scale (OAA/S scale) is a well-established instrument for evaluating the level of consciousness. The OAA/S scale was developed in 1990 to measure the level of consciousness in patients sedated with midazolam [6]; the scale is sensitive to the level of midazolam administered. A score of 3–4 on the OAA/S scale represents a moderate level of sedation-analgesia and a score of 1–2 represents unconsciousness (Table 1). Therefore, a score of more than 3 on the OAAS/S scale is required for MAC. However, some degree of patient stimulation, such as calling, prodding, or shaking, is required during the operation to evaluate the patient's level of sedation with the OAAS/S scale, and these assessments may affect sedation status. In addition, the results of the evaluation may be dependent on the assessor and fail to account for the changes in sedation level that may occur between assessments.

The Ramsay Sedation Scale (RSS) was introduced in 1974 as a subjective tool to evaluate the level of consciousness during titration of sedative medications in the intensive care unit [7]. The RSS assesses the level of consciousness, agitation, and anxiety through observation of behavior, and response to voice, a loud auditory stimulus or a light glabellar tap (Table 2).

Real time and continuous monitoring of the sedative level can be performed with electroencephalographic (EEG) methods such as the Bispectral Index (BIS). The BIS is an instrument used specifically for easy analysis of EEG variations, which correspond to different levels of sedation. Sedatives and analgesics specifically change the frequency and amplitude of EEG waves, which are analyzed and correlated with a numerical index by using the BIS [8]. In a study with the BIS and propofol sedation, the BIS reliably assessed the sedation depth achieved with propofol; a decrease in the BIS was associated with the incidence of amnesia during the operation [9].

Patient Satisfaction Score (Iowa Satisfaction with Anesthesia Scale)

The Iowa Satisfaction with Anesthesia Scale (ISAS) is a tool for measuring patient satisfaction during anesthetic experiences including MAC [10]. The ISAS is a self-administered, written questionnaire on which patients respond to 11 items on a six-choice, vertical answer column [10].

Systemic Sedatives and Analgesics

In addition to the use of local anesthetic drugs, systemic sedatives and analgesics are required to provide patients with comfort during surgical procedures performed with MAC. A pharmacological approach is required since there is a synergistic effect between sedation and analgesia. Continuous infusion of rapid elimination drugs helps the anesthesiologist achieve target drug concentrations at the effect-site, as well as maintain safety.

Several infusion regimens, including bolus injection, continuous infusion, target controlled infusion (TCI), and patient controlled sedation (PCS) can be used during MAC [1]. During continuous infusion, the velocity of the drug infusion can be determined by the attending anesthesiologist according to the patient's level of consciousness and clinical signs [1]. TCI calculates the infusion velocity to obtain and maintain specific plasma level or effect site concentration targets, based on the patient's pharmacokinetic parameters [1]. PCS allows patients to administer intravenous drugs and achieve a specific level of consciousness according to the requirement for more sedation and analgesia [1]. PCS was programmed by the anesthesiologist with a bolus injection and a lock out time to avoid over-sedation since there is wide variability in drug effects among patients.

The judgment and discretion of an experienced anesthesiologist are required for safety because the airway of the patient is

not secured; the infusion of sedatives and analgesics should be individualized during MAC. Monitoring devices are especially required for MAC outside of the operating room. According to previous reports, the severity of injury in claims after MAC was comparable to those pertaining to general anesthesia [11]. Respiratory compromise resulting from over-sedation was the most common cause of injury, and 41% of those claims were related to death or permanent brain damage [11]. Sedation related respiratory depression can be preventable with better monitoring, vigilance (of the attending anesthesiologist), and early resuscitation [11].

Geriatric anesthesia is increasing and MAC is an attractive option for many procedures to minimize the physiological stress of elderly patients. However, elderly patients show reduced functional reserve, including loss of normal compensation against the stress of cardiovascular and respiratory compromise, and altered mental status [12]. In addition, geriatric patients show different and variable pharmacokinetic responses to sedatives and analgesics due to changes in body composition and functions. Therefore, the attending anesthesiologist should administer the drugs while monitoring the consciousness level and hemodynamics [12].

Common causes of complications during infusion of sedatives and analgesics for MAC include airway obstruction, hypoxia, and cardiovascular collapse. In addition to local anesthesia administered by surgeons, sedatives and analgesics are co-infused and their synergistic effect results in complications. Inhibition of the airway reflex after infusion of sedatives and analgesics may lead to respiratory compromise, upper airway obstruction, and aspiration. Careful and continuous infusion of sedatives instead of intermittent bolus injection may minimize the risk of respiratory depression. In addition, oxygen delivery [13], as well as monitoring through capnography or thoracic impedance [5], are recommended to prevent and detect airway complications during drug administration.

Sedatives

Patients typically suffer from discomfort and anxiety during the procedure and sedatives are used for amnesia and anxiety relief. Proper concentrations of sedatives are required since light sedation may cause patient anxiety while heavy sedation leads to airway obstruction and compromise. The level of sedation can be monitored through patient communication and hemodynamic variables. Patients are cooperative without airway compromise during proper sedation. Using PCS, the infusion rate of sedatives can be individualized according to the patient's needs. Ideal characteristics of sedatives during MAC are rapid onset and recovery, easy titration, and minimal respiratory and cardiovascular depression. In addition, each procedure requires

a different level of sedation, which should be decided according to the type of surgery.

Benzodiazepines provide patient comfort and amnesia during the procedure; midazolam is the most commonly used benzodiazepine. Midazolam (starting dose: 0.03 mg/kg, infusion rate: 0.6–6.0 mg/kg/h) is typically co-injected with propofol [1]. It shows maximal CNS effects within 2–3 min; repeated or continuous injection within a relatively short period may lead to heavy sedation, which can be reversed with flumazenil.

Propofol remains the mainstay drug of MAC because of its favorable pharmacodynamic and pharmacokinetic profile. Compared with midazolam, cognitive function recovery is faster and the degree of postoperative sedation, dizziness, amnesia, and postoperative nausea and vomiting (PONV) are lower after propofol sedation [14]. However, propofol does not have an analgesic effect, and other opioid analgesics are often required during painful procedures [14].

Dexmedetomidine and clonidine are α2 agonists that inhibit endogenous catecholamine release in the locus ceruleus, which results in a sedative-analgesic effect without respiratory depression [15]. Dexmedetomidine is eight times more selective for the α2 receptor than clonidine. Due to its sedative properties, intravenous dexmedetomidine (1 μg/kg) relieves patient anxiety. In addition to its sedative effect, dexmedetomidine shows analgesic properties and reduces opioid requirements [15]. Since dexmedetomidine reduces the occurrence of respiratory depression, it is a useful sedative and analgesic during MAC. However, dexmedetomidine leads to hypotension and bradycardia due to the inhibition of catecholamine release [16]. Therefore, these adverse events should be considered for elderly patients with cardiovascular disease. The onset and offset of dexmedetomidine is slower than midazolam and the administration of dexmedetomidine to ambulatory patients should be individualized considering delayed recovery.

Analgesics

Analgesics are used during MAC to relieve the discomfort and pain associated with procedures. Fentanyl is one of the most commonly used analgesics during MAC, and fentanyl 50–100 μg has an onset of 3–5 min and duration of 45–60 min [17]. Even small amounts (25–50 μg) of fentanyl may cause respiratory depression if co-infused with other sedatives. Alfentanil can be injected intermittently to relieve procedure-associated discomfort and pain [18]. Remifentanil, an ultra-short-acting opioid with a rapid onset time (1 min) and short duration of action (3–10 min), is an ideal opioid for continuous infusion, and for managing pain related to surgical stimulation [3]. However, an anesthesia care provider should be cautious during remifentanil infusion since remifentanil often causes respiratory depression [3].

Ketamine is an N-methyl-o-aspartate receptor antagonist that has profound analgesic, sedative, and amnestic characteristics. Ketamine is a particularly valuable analgesic during MAC because it does not cause clinically significant respiratory depression or PONV. Low dose ketamine (0.25–0.50 mg/kg) with propofol has been used during ambulatory MAC for plastic surgery [19]. Ketamine-dexmedetomidine combination is known to be effective in sedation and analgesia for pediatric patients during magnetic resonance imaging [20].

Non-steroidal anti-inflammatory drugs (NSAIDs) such as ketorolac have analgesic properties. Compared with opioids, NSAIDs cause less adverse effects such as pruritus and PONV. Ketorolac has been used as an adjunct analgesic during local anesthesia or propofol infusion because it has lower analgesic effects than opioids [21].

Procedures Performed Under MAC

Eye surgery

Cataract surgery is typically performed under topical anesthesia [22]. Topical anesthesia is simple to perform and avoids the potential risk of retrobulbar or peribulbar nerve block. However, topical anesthesia may not provide complete analgesia and may cause discomfort and anxiety. For this reason, MAC with topical anesthesia and infusion of intravenous sedatives and analgesics can provide anxiety relief and patient comfort during cataract surgery [22].

Sedation with midazolam has been commonly used with topical anesthesia for cataract surgery. In a randomized, double-blind trial in patients with cataract surgery, dexmedetomidine was associated with slightly better patient satisfaction compared with midazolam [23]. However, dexmedetomidine group patients showed relative cardiovascular depression and delayed recovery [23]. Cardiovascular depression including bradycardia and hypotension should be considered during MAC for cataract surgery since patients with cataract surgery typically have comorbidities such as hypertension and diabetes mellitus. Another study compared dexmedetomidine with remifentanil during cataract surgery in patients under topical anesthesia; the result showed that surgeon satisfaction was lower for the dexmedetomidine group than for the remifentanil group because of poor cooperation and deep sedation of the patients [24].

In previous studies on cataract surgery-related adverse events, cataract surgery performed under topical anesthesia with MAC required anesthesiologist intervention in 21.6% of cases [25]. Agitation was more common in younger patients with neurological or psychiatric diseases, while hypertension was more common in older patients with higher ASA scores [25].

Otolaryngologic surgery

Surgeries that had previously been performed with only local anesthesia have since been performed with MAC due to it its advantages for patient safety and satisfaction. During tympanoplasty, surgeons provide local anesthesia on the surgical spot and the anesthesiologist infuses sedatives and analgesics [26]. Recently, dexmedetomidine has been investigated and compared with midazolam-fentanyl combination during tympanoplasty; the dexmedetomidine group had higher surgeon satisfaction scores than the midazolam-fentanyl group [26]. Percutaneous dilatational tracheostomy can be performed under local anesthesia, but MAC with midazolam, propofol, and alfentanil increased patient comfort and satisfaction [27] .

Inguinal herniorrhaphy

Inguinal herniorrhaphy is one of the most common surgical procedures performed under MAC in an ambulatory setting. A previous study reported that MAC with local anesthesia plus intravenous sedatives and analgesics resulted in more rapid recovery and lower medical costs than general anesthesia [28]. Spinal anesthesia and MAC with ilioinguinal-hypogastric nerve block plus remifentanil infusion were compared for inguinal herniorrhaphy: MAC was associated with hemodynamic stability, fewer side effects, and higher satisfaction than spinal anesthesia [29].

Cardiovascular procedures

Endovascular aortic aneurysm repair (EVAR) can be performed under general anesthesia, regional anesthesia, or MAC [30,31]. However, the use of general anesthesia for EVAR was related with increased postoperative hospital stay and respiratory compromise compared with regional or MAC [30,31]. In the majority of patients with transcatheter-aortic valve replacement, MAC was associated with a shorter procedure time and hospital stay than general anesthesia [32,33]. In this case, sedation should be performed by an experienced anesthesiologist and immediate conversion to general anesthesia should be prepared [32,33].

Pain procedures

MAC can be provided for patients with invasive percutaneous vertebroplasty or diagnostic imaging discography [34,35]. During percutaneous vertebroplasty, TCI with propofol provided satisfactory sedation and high operator satisfaction [18]. In a preliminary trial of dexmedetomidine for analgesia and sedation during diagnostic discography, dexmedetomidine was reported to be an adequate sedative and analgesic [34].

Gastroendoscopic procedure

MAC for gastro-endoscopic procedures is increasingly applied outside the operating room for operator and patient satisfaction. MAC for Gastro-endoscopic procedures should allow for safe sedation and complete examination, as well as rapid recovery. Especially, endoscopic retrograde cholangiopancreatography (ERCP) is a painful and long procedure in the lateral decubitus position, and MAC for ERCP procedures requires rather deep sedation and complete analgesia while allowing for respiratory and cardiovascular stability [36]. Conventionally, the combination of midazolam and meperidine or fentanyl has been used for MAC in ERCP because of the relative lack of respiratory depression; different drug combinations have been recently investigated and compared [37,38]. The addition of propofol or dexmedetomidine with this conventional regimen decreased the requirement for additional sedatives and increased operator satisfaction [37,38]. During MAC for ERCP, relative deep sedation is required and cardiovascular or respiratory complications. including arterial hypotension, desaturation, bradycardia, arterial hypertension, arrhythmia, and aspiration may occur [39]. For that reason, monitoring of the level of sedation, and the presence of a qualified anesthesiologist, are required for MAC in ERCP [39].

Flexible bronchoscopy

Flexible bronchoscopy is a diagnostic and therapeutic procedure typically performed under MAC. The ideal characteristics of sedatives during MAC, for flexible bronchoscopy, should allow the patient to maintain spontaneous ventilation and protect their own airway, while blunting sympathetic responses during bronchoscope insertion. The major safety concern with MAC for flexible bronchoscopy is excessive sedation depth and duration of hypoxemia. In addition, other indicators of cardiovascular instability, such as hypotension, hypertension, bradycardia, and tachycardia, should be considered during MAC for flexible bronchoscopy.

The combination of midazolam and hydrocodone was shown to reduce cough during flexible bronchoscopy without causing significant desaturation [40]. The combination of propofol and alfentanil during flexible bronchoscopy resulted in greater respiratory depression than propofol alone [41]. The major advantage of ketamine use is preservation of airway patency and respira-

tory function. Ketamine was superior to alfentanil when used in combination with propofol because of the high patient satisfaction and amnesia [42]. The safety profiles and efficacies of remifentanil and dexmedetomidine for sedation during flexible bronchoscopy have been investigated, with the results suggesting that dexmedetomidine was associated with a lower incidence of oxygen desaturation and reduced need for oral cavity suction than remifentanil during MAC for flexible bronchoscopy [43]. However, dexmedetomidine seemed to be less effective than remifentanil in that the dexmedetomidine group showed lower bronchoscopist satisfaction scores and more frequent need for topical anesthesia than the remifentanil group [43].

Neurosurgery

Patients should be awake and cooperative under MAC to monitor neurologic functions during awake craniotomy [44]. In such patients, adequate analgesia and sedation without respiratory and hemodynamic depression are required during application of the head frame, skin incision, and craniotomy, and the patient should be awake and cooperative for evaluation of neurologic functions during brain mapping and tumor resection [45]. In addition to scalp blocks, short half-life drugs such as propofol and remifentanil should be titrated, according to the surgical procedure step, by experienced anesthesiologists during awake craniotomy performed under MAC [44,45].

Conclusions

Diagnostic or therapeutic procedures in and outside of the operating room are increasing and MAC is preferred to general or regional anesthesia due to its cost-effectiveness and rapid recovery. Systemic sedatives and analgesics should be infused carefully after monitoring the patient's level of consciousness and hemodynamic variables, since heavy sedation may lead to central respiratory depression or airway obstruction. MAC should be chosen as a proper anesthetic alternative after patient co-morbidities and preferences, and the type of procedure being performed, have been considered. The choice of sedative and analgesic is based on the required depth of sedation and analgesia of each procedure. The presence of a sufficiently experienced anesthesiologist, as well as oxygen supply, monitoring devices and emergency equipment, are required during MAC both in and outside the operating room.

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