



Sedation and Anesthesia for Cardiology Procedures

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Abstract

Many cardiology procedures require sedation and/or anesthesia, so it is important that the practicing physician be familiar with the use of the pertinent medications to ensure patient safety. Preoperative risk stratification and Mallampati assessments are routinely performed to optimize care. As the field of interventional cardiology continues to develop, the number of invasive procedures performed is expected to grow, requiring more providers to become familiar with sedation/anesthesia for these procedures. In this review article, we discuss the pertinent sedatives, anesthetics, medication dosing, reversal agents, common side effects and routine preoperative assessment methods.

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Introduction

Many cardiology procedures require the use of sedation and anesthesia. These include procedures like Transesophageal Echocardiography (TEE), Percutaneous Coronary Interventions (PCI) and Transcatheter Aortic Valve Replacements (TAVR), which are performed almost daily in major cardiology programs. Sedation and anesthesia are essential to ensure a safe procedural environment and patient satisfaction. The choice of sedative agent varies based on a number of factors including type of procedure, case complexity, expected duration, and

individual patient preoperative risk. Once the desired level of sedation has been determined, a variety of medications is available to choose from. Typical medication classes include local anesthetics, benzodiazepines, opioids, antihistamines, dissociative agents and propofol. Currently, the American College of Cardiology (ACC), American Heart Association (AHA), and the Society of Cardiovascular Angiography and Interventions (SCAI) have no definitive guidelines regarding anesthesia or sedation during cardiology procedures. Here, we have reviewed the several options for sedation and anesthesia, medication dosing, medication reversal and preoperative patient risk assessment.

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Local anesthesia

Local anesthetics act by competitive antagonism on the alpha subunit of voltage gated sodium channels in the nerve membrane. Additionally, anesthetic effects are gained by interaction with G protein coupled receptors and inhibition of calcium and potassium channels. The local anesthetic agents fall into two broad groups: amino ester and amino amide. The amino ester agents are procaine, tetracaine and benzocaine. The most common amino amide agent used is lidocaine. It is typically administered in the form of a subcutaneous injection during invasive cardiology procedures due to its rapid onset (3-5 minutes), short duration of action (30-60 minutes) and minimal risk of cardiotoxicity [34]. Although lidocaine is the local anesthetic of choice during cardiac catheterization, many other options are available. mepivacaine, bupivacaine and ropivacaine are viable alternatives in cases of lidocaine allergy. Of note, there is no documented evidence for true IgE mediated allergic reactions to lidocaine. However, reactions may occur to any vasoconstrictor additive or preservative present. So, the lowest risk of any reaction would be with the use of its preservative free form (MPF or methylparaben free) without any vasoconstrictor additive. Non-injectable forms of local anesthetic are also utilized [1]. Viscous lidocaine and benzocaine spray may be used to numb the posterior pharynx prior to TEE. Although rare, methemoglobinemia and cyanosis may occur with these compounds, risks increase if used in combination. Caution must be exercised to avoid cardiotoxicity, specifically with bupivacaine and ropivacaine. Due to the effects on the sodium channels, toxicity may result in conduction abnormalities (widened PR or QRS complex, bradycardia, heart block) and negative inotropy. The maximum acceptable dose is 5 mg/kg of lidocaine, 5 mg/kg of mepivacaine, 2 mg/kg of bupivacaine and 2.5 mg/kg of ropivacaine. [37,38]. The most rapid onset is lidocaine and most potent is bupivacaine [35]. Duration of action is longest with bupivacaine and shortest with lidocaine and mepivacaine [1-2,36].

Sedation

The American Society of Anesthesiologists (ASA) classifies sedation into four categories; (1) Minimal Sedation (Anxiolysis), (2) Moderate Sedation (Conscious Sedation), (3) Deep Sedation and (4) General Anesthesia. Minimal Sedation (Anxiolysis) is defined as a drug-induced state during which patients respond normally to verbal commands. Although cognitive function and physical coordination may be impaired, airway reflexes, ventilatory and cardiovascular functions are unaffected [3]. Anxiolysis is typically achieved with benzodiazepines, like midazolam, during cardiac catheterization. Moderate Sedation (Conscious Sedation) is defined as a drug-induced depression of consciousness during which the patient is able to respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation. No interventions are required to maintain a patent airway and spontaneous ventilation is adequate.3 Moderate sedation is the preferred level of sedation for cardiac catheterization. Deep Sedation is a drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully after painful or repeated stimulation (shoulder rub, sternal rub, etc.). The ability to independently maintain ventilatory function may be impaired. Patients may require assistance in maintaining a patent airway, and spontaneous ventilation may be inadequate [3]. During more involved cardiology procedures, a combination of benzodiazepines, opiates and Propofol can be used to achieve moderate sedation [4]. General Anesthesia is a drug-induced loss of consciousness

during which patients are not arousable and the ability to independently maintain ventilatory function is impaired. Patients require assistance in maintaining a patent airway and positive pressure ventilation is required [3]. Common agents used for general anesthesia include propofol, ketamine, etomidate and the volatile gases (halothane, isoflurane, desflurane, sevoflurane). It is recommended that providers administering general anesthesia be prepared to reverse the effects in cases of hemodynamic or respiratory instability [4]. For that reason, cardiology procedures that require general anesthesia should be assisted by an anesthesiologist.

Midazolam

Benzodiazepines provide Anxiolysis by effects on the Gamma-Aminobutyric Acid (GABA) and chloride channels of the cell, in effect producing greater flow of chloride ions through the cell reducing cell excitability [5]. The benzodiazepine of choice during cardiology procedures is midazolam, also known as Versed [6,7]. Midazolam is preferred because of its quicker onset of action (2-3 minutes), shorter duration time and mild anterograde amnesia [5,7]. Midazolam is a lipophilic benzodiazepine which allows it to enter the central nervous system quicker. Pharmacokinetics of intravenous midazolam typically results in a volume of distribution at around 1-2.5 L/kg, with a half-life ranging from 1-4 hours as it is rapidly metabolized by the liver through the cytochrome P450-3A4 system [5]. Midazolam dosing usually starts at 1 mg intravenously and it is then titrated to the desired effect [8]. In terms of cardiotoxicity, it is relatively safe and has no major effects on hemodynamics [9,10]. Respiratory status though should be monitored closely as respiratory depression can occur due to its depression of central nervous system function [5]. An additional effect may be post procedural delirium, which should be considered in elderly patient [11]. If necessary, reversal can be achieved with flumazenil, a GABA receptor antagonist. Flumazenil is administered with a starting dose of 0.2 mg which can be titrated up by 0.1-0.2 mg/min, to a total maximum dose of 1 mg [8,12].

Fentanyl

Like benzodiazepines, opioids may also be used for Anxiolysis. They also possess analgesic properties but lack amnestic effects [13]. Opioids can be combined with benzodiazepines to produce Anxiolysis, analgesia, and amnesia in the patient [13]. Fentanyl in combination with midazolam are preferred agents for sedation and analgesia during cardiac catheterization, particularly using radial access, since they have been shown to reduce radial artery spasm through endothelial relaxation [14]. Fentanyl is a mu receptor agonist which causes hyperpolarization of the cell by allowing presynaptic influx of calcium and postsynaptic efflux of potassium [15]. Fentanyl is highly lipophilic which allows it to enter the central nervous system at a faster rate. The half-life of fentanyl is estimated to be between 1.5 and 7 hours and it is metabolized by the liver through the CYP3A5 and 3A7 pathways [15]. Recommended dosing for Fentanyl is 12.5 to 50 mcg intravenously and this can be repeated every 3 to 5 minutes as needed [8]. In terms of potential side effects, Fentanyl can cause muscular rigidity, hypoventilation, respiratory depression and hypoxia [7, 16-17]. In select cases, higher doses of Opioids can cause hypotension and bradycardia [16,17-18] In the context of cardiovascular care, Fentanyl can also interact with P2Y12 inhibitors, slowing the rate of absorption of those drugs [19]. Opioid reversal can be achieved with naloxone, an opioid antagonist, at doses of 0.2 to 2 mg. The onset of reversal occurs in 2 to 3 minutes if given intravenously

[8]. Slow administration is recommended, unless the level of sedation is causing hemodynamic compromise or respiratory distress, in order to avoid the effects of rapid reversal. Additional doses may be required as it has a duration of 20 to 40 minutes and a half-life of 30 to 90 minutes [20,21]. Rapid reversal can cause withdrawal symptoms, which include elevated blood pressure and respiratory rate [21].

Diphenhydramine

Antihistamines (reversible H1 receptor inhibitors) can be used as an adjunct to the usual anesthetics and sedatives. They can be divided into two classes, first and second generation. First generation antihistamines include diphenhydramine, chlorpheniramine and dimenhydrinate. These antihistamines are typically used to treat allergic reactions, motion sickness and in certain circumstances for insomnia due to their sedating effects [22]. Side effects of first-generation antihistamines include antimuscarinic and anti-alpha adrenergic effects. Second generation antihistamines contain fewer sedating properties compared to first generation antihistamines due to decreased central nervous system penetration. These agents include cetirizine, loratadine, desloratadine and fexofenadine. Among the first-generation antihistamines, diphenhydramine, is sometimes used for adjunct sedation during cardiology procedures [11], particularly when the patient reports a past history of contrast reaction. Dosing usually starts at 12.5 to 25 mg IV and this can be repeated until the desired effect is achieved. It can take up to 2 hours to reach peak effect and the half-life can vary between 3 and 9 hours as it is metabolized extensively via the CYP2D6 pathway [22]. Caution must be taken when administering antihistamines, as there is a relative lack of titratability, long duration of action, variable effect and lack of reversal agents.

Propofol

Additional agents are frequently required for some procedures (TEE, cardioversion, ablations, TAVR, etc.) that require a higher level of patient sedation [23,24]. Numerous studies have reported the benefit of using Propofol for certain cardiology procedures. Compared to sedation with midazolam, Propofol has a shorter time to onset and faster recovery time [7,25,26]. Dosing for healthy adults is calculated in accordance with adjusted body weight. Initial dosing used for cardiology procedures is 0.5 to 1 mg/kg, followed by 0.25 to 0.5 mg/kg every 1 to 3 minutes. When given in intermittent boluses, 10 to 20 mg is typically adequate to achieve moderate sedation. Onset of action is less than 1 minute but this can vary due to dose dependence. Half-life is approximately 40 minutes, although it may take up to 7 hours (terminal half-life). Eventual clearance is 60% achieved through hepatic metabolism and 40% extrahepatic clearance, majority of which is accomplished through the kidneys. Caution must be taken to avoid adverse effects, which include hypotension, QT interval prolongation, myoclonus, and apnea [27]. Hypotension is most severe in those patients with reduced left ventricular systolic function. Titration must also be performed with caution, as the therapeutic index is narrow, and patients may transition from deep sedation to general anesthesia if overdosed.

Ketamine

A dissociative agent may be used to aid with procedural sedation. While midazolam helps reduce dysphoria, ketamine can cause it. Ketamine is the most commonly selected dissociative agent for cardiology procedures. Ketamine has recently gained

recognition in the cardiac catheterization lab due to its ability to produce amnesia, analgesia and sedation. It also allows for preservation of laryngeal and pharyngeal reflexes, spontaneous respiration and has minimal effects on blood pressure. In fact, some studies have found a mild cardiac stimulatory effect, which can improve blood pressure, atrial contraction, and heart rate during procedures [28]. Dosing of ketamine when used for procedural sedation is 1 to 2 mg/kg over a minute. Additional dosing may be provided every 5 to 10 minutes at 0.5 to 1.0 mg/kg. Onset of action is almost immediate when administered intravenously. It is metabolized in the liver and has a half-life of approximately 45 minutes [29].

Pre-procedural assessment

A proper evaluation of the patient prior to the procedure is necessary to ensure safety.

ASA physical status classification system

The ASA has created a six-class physical status assessment which has been widely adopted as part of the pre-procedural assessment [30]. Class I is defined as a normal healthy patient. Class II is a patient with mild systemic disease (i.e., patients with hypertension or diabetes without end organ damage, active smoker). Class III is a patient with severe systemic disease (i.e., patients suffering from angina or who have had recent myocardial infarction greater than 3 months ago). Class IV is a patient with severe systemic disease that is a constant threat to life (i.e., patients with advanced heart failure, recent myocardial infarction within 3 months, severely reduced ejection fraction or end stage obstructive pulmonary disease). Class V is a moribund patient who is not expected to survive without prompt medical-surgical intervention (i.e., a ruptured aortic aneurysm, massive pulmonary embolism, acute myocardial infarction). Class VI is a patient who has been declared brain-dead whose organs are being evaluated for procurement [31].

Mallampati classification system

The Mallampati Classification system was created as a tool to assess airway prior to potential intubation [32]. This system uses mouth opening and tongue size to estimate the amount of space available to place a direct laryngoscope [32]. This system divides patients into four classes. Class I predicts easy intubation as patients have complete visualization of the soft palate and uvula. Class II is also associated with successful intubation as most of the soft palate is visualized and complete visualization of the uvula is still present. Class III is usually associated with a more difficult intubation as only the base of the uvula is visualized. Class IV presents the most difficult intubation, as the soft palate and uvula are not visible [33].

Conclusion

As the field of interventional cardiology continues to grow, invasive procedures will only become more common. Thus, a thorough understanding of sedation, anesthesia and pre-procedural assessment will become a crucial and necessary aspect of all cardiovascular care.

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