Introduction to moderate and deep sedation

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History of sedation

Some have argued that the development of sedation and analgesia may be one of the preeminent advances in both medical science and human technology. The power to manipulate and alter human consciousness and perception of pain has opened the door to extraordinary possibilities for medical practice. However, the origins of these advances reach far back to the limits of written history. Ancient Greeks recognized that naturally occurring substances such as mandrake root and alcohol could alter consciousness and be used during surgical manipulations [1,2]. Inca shamans used coca leaves to assist in trephination operations in which burr holes drilled into the skull were thought to cure illnesses [1]. And surgeons in the Middle Ages used ice and so-called “refrigeration anesthesia” to dull pain sensation prior to incision [2,3].

The modern practice of sedation is the end result of a process of evolution in alteration of consciousness, likely starting with the discovery of the analgesic properties of ether [1,4]. A medical student from Rochester, New York, named William Clarke used ether during a tooth extraction in January 1842. Many believe that this procedure may have been the first successful use of ether. Sedative technique using ether was further developed by Crawford Long during a neck tumor excision [1,4,5]. Later in 1842, Horace Wells would be the first to give a public demonstration at Massachusetts General Hospital. Unfortunately, when the patient cried out in pain, he was ridiculed and the use of ether was called “humbug” [1,4,5]. William Morton later would return to the same “Ether Dome” at Massachusetts General Hospital to successfully demonstrate the use of ether [1,5,6].

Over the years, the practice of sedation/analgesia has evolved significantly. Some patients prefer sedation to general anesthesia, and they often feel less anxious about receiving the former. Indeed, many healthcare practitioners prefer sedation because it offers a rapid return to pre-sedation condition and because of other patient, provider, and procedure-related factors.

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History of sedation

Definitions of sedation

Involvement and regulation of nurses practicing sedation

Summary

References
### Table 1.1. Procedures performed under sedation administered by non-anesthesia-trained professionals

<table>
<thead>
<tr>
<th>Head and neck</th>
<th>Superficial thoracic</th>
<th>Extremity procedures</th>
<th>Gastrointestinal/abdominal</th>
<th>Vascular</th>
<th>Gynecologic/urologic</th>
<th>Emergency department/radiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dental extractions</td>
<td>Breast augmentation</td>
<td>Carpal tunnel release</td>
<td>Endoscopic retrograde cholangiopancreatography</td>
<td>Hemodialysis access placement</td>
<td>Diatation and curettage</td>
<td>Reduction of dislocation or fracture</td>
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<td>Blepharoplasty</td>
<td>Breast biopsy</td>
<td>Trigger finger release</td>
<td>Colonoscopy</td>
<td>Pacemaker insertion</td>
<td>Fulguration of vaginal lesions</td>
<td>Complex suturing</td>
</tr>
<tr>
<td>Rhytidoplasty</td>
<td>Bronchoscopy</td>
<td>Removal of pins/wires/screws</td>
<td>Endoscopic ultrasound</td>
<td>Angiography</td>
<td>Fulguration of anal lesions</td>
<td>Insertion of elective chest tube</td>
</tr>
<tr>
<td>Rhinoplasty</td>
<td>Chest tube insertion</td>
<td>Closed reduction</td>
<td>Gastroscopy</td>
<td>Cardiac catheterization</td>
<td>Cystoscopy</td>
<td>MRI</td>
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<td>Laceration repair</td>
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<tr>
<td>Cataract extraction</td>
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</table>

- **Head and neck**
- **Superficial thoracic**
- **Extremity procedures**
- **Gastrointestinal/abdominal**
- **Vascular**
- **Gynecologic/urologic**
- **Emergency department/radiology**
Recently, the definitions of “general anesthesia” and “sedation” have undergone a period of development, leading to further characterization of the two techniques as distinct. It should be recognized that practitioners of early dental and oral maxillofacial surgery were at the forefront of developing the practice of sedation [6]. By the 1980s, most sedation of healthy patients for such dental procedures was administered by a registered nurse (RN), supervised by the physician, using benzodiazepine with an opioid [4].

One of the central questions surrounding the practice of sedation relates to who should administer it. Many agree that the individuals most trained in the administration of sedative/hypnotic drugs, airway management, and patient resuscitation should administer sedation. Unfortunately, the demand for such providers is significantly greater than the supply. Therefore, many different providers, from physicians to registered nurses to physician assistants, provide sedation in today’s healthcare milieu. Additionally, a broad spectrum of procedures have been carried out under sedation administered by non-anesthesia-trained registered nurses (Table 1.1) [7].

As the technology and practice of sedation and monitoring have evolved, the scope of practice of many providers has expanded. With time, sedative techniques have transitioned out of the operating room and into more diverse locations. Procedures have become shorter and less invasive, and technology and medical science have advanced. Furthermore, persons administering and managing sedation for a patient have diversified in tandem. Procedural sedation has been administered by anesthesiologists, certified registered nurse anesthetists (CRNAs), registered nurses, medical technicians, physician assistants, dentists, surgeons, and even by patients themselves (with supervision). Sedation is more attractive than general anesthesia to many stakeholders because it offers a potentially shorter recovery time, requires limited airway management, requires fewer personnel, is often more cost-effective, and may result in better patient satisfaction [8,9,10].

Recent technological advances have drastically changed the practice of sedation. One of the most significant was certainly the development of pulse oximetry during World War II by Glen Millikan [11]. Using optics to monitor the hemoglobin oxygen saturation provides a wealth of information to the clinician. This development has revolutionized the safety of sedation.

Another critical milestone has been the evolution of sedative medications. Early sedative drugs generally had a slower onset and longer duration of action than many modern drugs, as well as many undesirable side effects. Over time, new agents were discovered or developed that reduced these limitations. One of the most common sedative medications is midazolam [12]. The popularity of this drug is likely due to its quick onset, short duration of action, and favorable safety profile. It lacks analgesic properties but can cause desirable amnesia. Propofol can be used to induce general anesthesia, but subhypnotic doses have benefits of titratable sedation with rapid onset/offset. Its antiemetic properties are especially beneficial in the ambulatory setting, but it should be noted that it lacks analgesic effects [7,12]. Currently, the opioid of choice for sedation analgesia for many practitioners is fentanyl. Again, this popularity is likely related to its potency and short duration of action, such that it can be administered quite safely by an experienced practitioner [7,12,13].

Definitions of sedation

In 2002, the American Society of Anesthesiologists (ASA) appointed a task force to update practice guidelines for non-anesthesiologists administering sedation and analgesia. Levels
of sedation/anesthesia were defined according to responsiveness, airway, spontaneous ventilation, and cardiovascular function, as shown in Table 1.2 [14].

The levels of sedation presented in Table 1.2 are useful only if there are agreed-upon definitions of the different levels of consciousness. The ASA defines these levels as follows [14]:

(1) **Minimal sedation (anxiolysis)** – a drug-induced state during which patients respond normally to verbal commands. Although cognitive function and coordination may be impaired, ventilatory and cardiovascular functions are unaffected.

(2) **Moderate sedation/analgesia (conscious sedation)** – a drug-induced depression of consciousness during which patients 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. Cardiovascular function is usually maintained.

(3) **Deep sedation/analgesia** – a drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully following repeated or painful stimulation. 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. Cardiovascular function is usually maintained.

(4) **General anesthesia** – a drug-induced loss of consciousness during which patients are not arousable, even by painful stimulation. The ability to independently maintain ventilatory function is often impaired. Patients often require assistance in maintaining a patent airway, and positive pressure ventilation may be required because of depressed spontaneous ventilation or drug-induced depression of neuromuscular function. Cardiovascular function may be impaired.

The ASA further states that it is not always possible to predict how an individual patient will respond to a particular sedation plan. If a patient’s level of sedation progresses to a stage that is deeper than originally planned, the practitioner should be able to rescue the patient from the

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**Table 1.2. Continuum of depth of sedation: definitions of general anesthesia and levels of sedation/analgesia**

<table>
<thead>
<tr>
<th></th>
<th>Minimal sedation</th>
<th>Moderate sedation/analgesia (&quot;conscious sedation&quot;)</th>
<th>Deep sedation/analgesia</th>
<th>General anesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Responsiveness</strong></td>
<td>Normal</td>
<td>Purposeful&lt;sup&gt;a&lt;/sup&gt; response to verbal or tactile stimulation</td>
<td>Purposeful&lt;sup&gt;a&lt;/sup&gt; response after repeated or painful stimulation</td>
<td>Unarousable even with painful stimulus</td>
</tr>
<tr>
<td><strong>Airway</strong></td>
<td>Unaffected</td>
<td>No intervention required</td>
<td>Intervention may be required</td>
<td>Intervention often required</td>
</tr>
<tr>
<td><strong>Spontaneous ventilation</strong></td>
<td>Unaffected</td>
<td>Adequate</td>
<td>May be inadequate</td>
<td>Frequently inadequate</td>
</tr>
<tr>
<td><strong>Cardiovascular function</strong></td>
<td>Unaffected</td>
<td>Usually maintained</td>
<td>Usually maintained</td>
<td>May be impaired</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reflex withdrawal from a painful stimulus is not considered a purposeful response.

Source: American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists [14].

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4 Chapter 1: Introduction to moderate and deep sedation
deeper level of sedation. For example, individuals who administer moderate sedation/analgesia (formerly known as “conscious sedation”) should be able to rescue patients who enter a state of deep sedation/analgesia, and those administering deep sedation/analgesia should be able to rescue patients who enter a state of general anesthesia [14]. It is important to emphasize that general anesthesia does not necessitate endotracheal intubation: one can administer general anesthesia, as defined by the ASA, without any airway device in place. Finally, there is a distinction between moderate sedation/analgesia and monitored anesthesia care (MAC). Specifically, the ASA defines MAC as “the anesthesia assessment and management of a patient’s actual or anticipated physiological derangements” that may occur during the procedure. Furthermore, the provider of MAC must be qualified to convert to general anesthesia and rescue the patient’s airway, and must be trained in all aspects of anesthesia care [15].

With the tremendous growth in the number and complexity of procedures, sedation has expanded in practice to many non-anesthesia and non-physician practitioners. Many professional organizations have established their own practice guidelines and standards (see Guidelines and Standards, XIV). For example, the ASA guidelines specify recommendations in the following areas [14]:

1. patient evaluation
2. pre-procedure preparation
3. monitoring in regard to level of consciousness, pulmonary ventilation, oxygenation, and hemodynamics
4. recording of monitored parameters
5. availability of an individual responsible for monitoring
6. training of personnel
7. availability of emergency equipment
8. use of supplemental oxygen
9. combinations of sedative–analgesic agents
10. titration of agents
11. anesthetic induction agents used for sedation/analgesia (propofol, ketamine)
12. intravenous access
13. reversal agents
14. recovery care

Involvement and regulation of nurses practicing sedation

In the USA, there is little in the way of federal regulation with regard to scope of practice issues for registered nurses practicing sedation, so many look to state boards of nursing for regulation. Thus, there is much variability in the limitations placed on nurses practicing sedation across the United States. Nevertheless, the Association of periOperative Registered Nurses (AORN) has produced guidelines for what every registered nurse should know about “conscious sedation.” These published recommended practices provide guidelines for who manage the care of patients during sedation/analgesia [16].

According to the AORN, moderate sedation/analgesia is “produced by the administration of amnesic, analgesic, and sedative pharmacologic agents.” Furthermore, “moderate sedation/analgesia produces a condition in which the patient exhibits a depressed level of consciousness and an altered perception of pain but retains the ability to respond appropriately to verbal and/or tactile stimulation and maintains protective reflexes” [16].
The desire to lend safety to the practice of non-anesthesia RNs has led many state nursing boards to develop acceptable practices for such providers. In turn, each individual institution will use these guidelines to produce its own sedation protocols in accordance with state law. All nurses participating in the administration of sedation and analgesia should periodically review most recent policies and procedures in their respective state and institution.

Outside of state law, there are a number of nonlegal organizations that develop position statements and practice guidelines. These are frequently used in concert with state law to develop individual sedation policies. Position statements are developed by a panel of experts and, in the absence of clinical evidence, are based largely on expert opinion. Practice guidelines are systematically developed and evidence-based, and are designed to assist the practitioner in making clinical decisions on a day-to-day basis. Such guidelines should be clear and free of bias. Finally, “recommended practices” represent an organization’s official position on an issue and, in this case, are considered “statements of optimum performance criteria on various aspects of technical and professional perioperative nursing practice” [15].

Knowledge of these regulatory issues is important. In the case of malpractice proceedings, all of the above-mentioned guidelines are used to develop a standard of care, which is considered to be what a reasonable, equivalent practitioner would do in a given situation. In order to be convicted of malpractice, one must not have met the standard of care. Thus, all practitioners should be familiar with guidelines relevant to their practice.

With the ever-widening scope of sedation, practitioners must recognize the importance of standardizing practice. Organizing bodies such as the ASA, the AORN, the American Association of Nurse Anesthetists, the Society for Gastrointestinal Nurses and Associates, the American Society of PeriAnesthesia Nurses, the Emergency Nurses Association, and the American Association of Critical Care Nurses are constantly updating and releasing practice guidelines for those who practice sedation (see Guidelines and Standards, XIV). Furthermore, in the United States, most state governments use these guidelines to regulate practice through legislation. The Joint Commission also surveys all healthcare organizations to ensure that professional standards are maintained and protocols are followed in regard to administering sedation to patients [13,14,17]. Patient safety must be the number one priority for practitioners who administer sedation.

Summary
The practice of sedation has evolved significantly over the past 30 years. Once mainly the task of anesthesiology personnel, the demand for sedation services has outstripped the supply. The result has been the expansion of the scope of practice of other professionals. With continued attention to a high standard of safety, many different professionals are able to provide sedation services to those patients who need them.

References


Introduction

An increasing number of procedures requiring moderate and deep sedation are being performed outside the surgical suite. As a result, qualified non-anesthesia providers are administering moderate and deep sedation to patients for a variety of diagnostic, therapeutic, and/or surgical procedures. Practitioners should aim to provide patients with the benefits of sedation and/or analgesia while minimizing the associated risks. In order to do so, individuals responsible for patients receiving sedation and/or analgesia should understand the pharmacology of the agents being administered as well as the role of pharmacologic antagonists for opioids and benzodiazepines. Furthermore, combinations of sedative and analgesics should be administered as appropriate for the procedure being performed and the condition of the patient. Policies and standards regarding administration of sedation and analgesia by non-anesthesia providers are addressed elsewhere in the book. The following chapter focuses on the pharmacology of the drugs most commonly used to provide moderate and deep sedation and their available reversal agents.

Pharmacology basics

A drug that activates a receptor by binding to that receptor is called an agonist. An antagonist is a drug that binds to the receptor without activating the receptor and simultaneously prevents the agonist from stimulating the receptor. Synergism is when the effect of two drugs exceeds their algebraic sum. This is commonly seen with benzodiazepines.
and opioids when they are used in combination. Pharmacokinetic properties of a drug determine its onset of action and duration of drug effect. More specifically, pharmacokinetics describes the absorption, distribution, metabolism, and excretion of a drug (i.e., what the body does to the drug.) Pharmacodynamics describes the responsiveness of receptors to a drug and the mechanism by which these effects occur (i.e., what the drug does to the body). Individuals respond differently to the same drug, and often these different responses reflect the pharmacokinetics and/or pharmacodynamics among patients (Table 2.1).

Pharmacokinetics (determines onset of action and duration of drug effect) is affected by route of administration, absorption, and volume of distribution. Volume of distribution is influenced by characteristics of the drug including lipid solubility, binding to plasma proteins, and molecular size. Pharmacodynamics and pharmacologic drug effects are described in terms of dose–response curves, which depict the relationship between the dose of a drug administered and the resulting pharmacologic effect. Dose–response curves predict the effect of the drug on the patient with increasing dose. Titration of a drug should proceed based on expected pharmacodynamics of the drug given. Key considerations during titration of medications include appropriate choice for the patient’s condition (e.g., renal failure, liver failure, previous drug exposure), appropriate choice of incremental dosing (i.e., time and quantity), and periodic monitoring. Preexisting disease processes also effect elimination half-time, which is an important consideration when administering sedation. Elimination half-time is the time necessary for plasma concentration of a drug to decrease to 50% during the elimination phase. Because elimination half-time is directly proportional to volume of distribution and inversely proportional to its clearance, renal and hepatic disease (altered volume of distribution and/or clearance) effect elimination half-time. It is important to understand that elimination half-time does not reflect time to recovery from drug effects. Elimination half-time allows for an estimation of the time it will take to reduce the drug concentration in the plasma by half. After about five elimination half-times, a drug is nearly totally eliminated from the body. Therefore, drug accumulation is likely if dosing intervals are less than this period of time.

Context-sensitive half-time

Elimination half-time does not always explain duration of action of many drugs used in sedation, especially if multiple boluses or infusions are used. Context-sensitive half-time (CSHT) is defined as the time taken for blood plasma concentration of a drug to decline by 50% after a drug infusion has been stopped. The “context” refers to the duration of the

| Table 2.1. Causes of variability of individual responses to a drug |
|-----------------|-----------------|
| 1. Drug interactions | Age |
| 2. Pharmacokinetics | Renal function |
| | Hepatic function |
| | Cardiac function |
| | Bioavailability |
| | Body composition |
| 3. Pharmacodynamics | Genetic differences |
| | Enzyme activity |
infusion of the drug. Figure 2.1 shows examples of several classes of drugs (benzodiazepines, opioids, barbiturates, propofol) with their CSHT (minutes) plotted against duration of infusion (hours). As depicted in this representative graph, several hours of continued infusion or multiple repeated boluses given at close intervals can result in significant accumulation of the active drug in the patient. This can lead to exaggerated side effects (sedation, respiratory depression) and delayed recovery. Therefore, it is prudent to take CSHT of the drug into consideration, especially during longer (> 2 hour) procedures, and also to keep track of the total amount of drug(s) given by adding up all the boluses and/or infusions.

Synergy effects

Drugs used in sedation can have synergistic (i.e., additive) effects. This presents both advantages and disadvantages for the practitioner. The advantage is that one can achieve the desired level of sedation by using several agents while minimizing the total amount of each. For example, fentanyl has analgesic properties while midazolam is more useful as a sedative and an anxiolytic drug. On the other hand, when these drugs are administered together, it can lead to exaggerated sedation and respiratory effects. Therefore, titration to effect and close monitoring are needed. Table 2.2 shows commonly used drug classes and their relative effects on sedation, anxiety, and pain, and on the cardiovascular and respiratory systems.

Routes of administration

Routes of administration include parenteral (intravenous, intramuscular, inhalational) and enteral (oral, rectal, nasal). For the purposes of moderate and deep sedation, intravenous administration is perhaps most useful. Drugs administered by the intravenous (IV) route generally have a more rapid onset than those administered by the intramuscular (IM) route. Intravenous sedative/analgesic drugs should be given in small, incremental doses titrated to desired end points of sedation and analgesia, with adequate time allowed between doses to achieve those effects. Ideally, each component should be administered individually to