Oral & Inhalational Sedation:

An Update and Refresher Course

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Our Clinicians:

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Dr. Mark Donaldson received his baccalaureate degree from the University of British Columbia, and his Doctorate in Clinical Pharmacy from the University of Washington. He has further completed a residency at Canada’s largest tertiary care facility, Vancouver General Hospital, and is the current Director of Clinical Pharmacy Performance Services for VHA, living in Whitefish, Montana. Dr. Donaldson is a Clinical Professor in the Department of Pharmacy at the University of Montana in Missoula, and Clinical Associate Professor in the School of Dentistry at the Oregon Health & Sciences University in Portland, Oregon. He has a special interest in dental pharmacology and has lectured internationally to both dental and medical practitioners. He has spent the last seventeen years focusing on dental pharmacology and the art of dental therapeutics, and has become a leader in this field of study. Dr. Donaldson has a number of published works in the peer-reviewed literature and spent three years in Japan focusing on cross-cultural communication and internationalization. He currently serves on the Editorial Board for the Journal of the American Dental Association. He is board certified in healthcare management and is the current President of the American College of Healthcare Executives’ Montana Chapter. Dr. Donaldson is the 2016 recipient of the AGD’s Dr. Thaddeus W. Weclew Award.

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Continuing Dental Education

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Question?!

1. What was the first drug presumably used for oral sedation?
   a. Benzodiazepines
   b. Barbiturates
   c. Alcohol
   d. Nitrous Oxide
   e. Opioids

2. What is the goal of minimal oral sedation?
   a. To put the patient to sleep
   b. To shut the patient up
   c. To reduce anxiety
   d. To facilitate coping

3. What organ is chiefly responsible for drug metabolism?
   a. Stomach
   b. Liver
   c. Kidney
   d. Blood
   e. Intestines

4. What basic equipment must you have to perform minimal oral sedation?
   a. Emergency drugs
   b. Positive pressure oxygen
   c. Pulse oximeter
   d. Automated external defibrillator

5. After delivering minimal oral sedation to a patient for a dental appointment, when is the patient ready to be dismissed?
   a. When they are awake
   b. After they have paid their bill
   c. When the drugs have worn off
   d. When they are ambulatory
   e. When sedation has waned
Mastering Adult Minimal Sedation: Oral and Inhalational Techniques
Jason H. Goodchild, DMD

Why is this talk important to you?
- Oral sedation is a hot topic in dentistry
- You may see advertisements for CE courses
- Your patients might see or hear advertisements for oral sedation
- It works!

Updates to the ADA Sedation and Anesthesia Guidelines: (first introduced in 1971)
  2005: Anxiolysis & Conscious Sedation
  2007: Minimal & Moderate Sedation
  2012: They updated some definitions
  2016: Updated Guidelines!

The course manual is intended to follow the agenda and slides. Additional information and reference reading is given in your workbooks!

Other Notes or Questions to Ask:
Definitions
(Source: ADA teaching and use guidelines for sedation and general anesthesia, October 2016)

Enteral – any technique of administration in which the agent is absorbed through the gastrointestinal (GI) tract (i.e., oral, rectal, sublingual)

Parenteral – a technique of administration in which the drug bypasses the gastrointestinal (GI) tract (i.e., IM, IV, intranasal, SM, SC, IO)

Minimal Sedation - a minimally depressed level of consciousness, produced by a pharmacological method, that retains the patient's ability to independently and continuously maintain an airway and respond NORMALLY to TACTILE stimulation AND verbal command. Although cognitive function and coordination may be modestly impaired, ventilatory and cardiovascular functions are unaffected.

Dosing for minimal sedation via the enteral route – minimal sedation may be achieved by the administration of a drug, either singly or in divided doses, by the enteral route to achieved the desired clinical effect, not to exceed the maximum recommended dose.

Nitrous oxide/oxygen when used in conjunction with sedative agent(s) may produce minimal, moderate, deep sedation, or general anesthesia

Teaching Minimal and Moderate Sedation (Oct 2016)
- Nitrous oxide / oxygen sedation: 14 hrs with clinical component
- Minimal Sedation: 16 hrs plus clinically oriented experiences
- Moderate Sedation (either enteral or parenteral): 60 hrs plus administration of sedation for at least 20 individually managed patients

Important Point: The ADA makes Guidelines but your State Dental Boards make the Rules! – READ YOUR STATE RULES & REGULATIONS!


Other Notes or Questions to Ask:
Case Example...

C.O. 46 yo female
- Tx Plan: Complete extractions and insertion of full upper and lower immediate dentures
- Tx length: 5 hours
- MHx:
  - MVP with regurgitation
  - No meds
  - No Known Drug Allergies (NKDA)
  - Patient smokes 1 ppd x 25 years
- Preoperative Vitals
  - BP 127/82 mmHg
  - Pulse 80 bpm
  - SpO₂ 98%

Drug Regimen:
Triazolam 0.50 mg total

Why Oral Sedation?
- Many people require additional measures to minimize anxiety and fear
- Anxious and fearful patients underserved
  - Costs to the patient are typically less than IV sedation or general anesthesia
  - How many people in need? Up to 100M?
  - Not enough O.S. & Anesthesiologists. Out of approximately 190,000 dentists in the US, only 10,000 are OS and DA.

Other Notes or Questions to Ask:

Source: American Society of Anesthesiologists. Continuum of Depth of Sedation: Definition of General Anesthesia and Levels of Sedation/Analgesia (last amended on October 15, 2014) Available at: www.asahq.org

Other Notes or Questions to Ask:
Minimal Sedation & Sedative Agents

**Anxiolysis** is a minimal level of sedation whereby the patient has decreased anxiety to facilitate coping skills while retaining interaction ability (minimal sedation).

**Conscious sedation** is a moderate level of sedation whereby the patient retains their protective reflexes as well as their own airway, and can respond to physical and verbal stimuli (moderate sedation).


All things considered equal, the lower the sedation level, the less chance for a serious adverse event to occur. The adage, “go low and go slow” is an excellent philosophy for the practice of sedating dental patients.

Other Notes or Questions to Ask:
Who is a candidate for oral sedation?

**Good**
- Patients who have difficulty achieving profound local anesthesia
- Gaggers
- Fearful or anxious patients
- Patients needing longer procedures
- Helpful with invasive procedures

**Difficult**
- Patients with complex medical histories
- Patients taking medications which may cause adverse reactions
- Severely depressed patients
- Patients with a severe mental handicap
- Pregnant patients


**The Drugs**

The goal of conscious sedation dentistry is to create a patient who is calm, and comfortable enough to receive dental care, and who can maintain a patent airway without assistance. Medications used for anxiolysis or conscious sedation should carry an inherent margin of safety such that overdose or unconsciousness is unlikely.

Because there are many medications that are anxiolytic (reduces anxiety) and hypnotic (involves the induction and increase of sleep duration), there may be instances that alternate regimens may be indicated.

**Other Notes or Questions to Ask:**
The decision to use drugs other than triazolam should be based on the practitioners’ level of training and should take into account many factors. The factors that may influence drug selection include:

- Medical History
- Drug interactions
- Allergies
- Length of appointment
- Depth of sedation needed
- Adverse reactions

Medications used for minimal or moderate sedation should carry an inherent margin of safety such that overdose or unconsciousness is unlikely: “First, Do No Harm!” Anxiolytic and Sedative agents are not new to the practice of medicine. Alcohols have been used for centuries to “numb” the mind to both painful as well as anxiety producing procedures. The use of opium has been traced back to Ancient Egypt. In the nineteenth century, drugs such as bromide (1853), chloral hydrate, paraldehyde, urethane and sulfonal (all pre-1970) were employed with varying degrees of success. Early in the twentieth century, the barbiturates were discovered (Barbital – 1903 and Phenobarbital – 1912), and the age of modern anesthesia was born. While these early drugs were effective, their level of safety was questionable.

Safety of a given medication can be measured pharmacologically by determining the **Lethal Dose 50 (LD50)**. The LD50 is that dose of a given drug that will result in mortality of 50% of the population when administered. Likewise, the **Effective Dose 50 (ED50)** is the dose of a given drug that will cause the desired results in 50% of a population.

The two terms can be related to one another by the Therapeutic Index (TI = LD50/ED50), which is a relative measurement of drug safety. The greater the Therapeutic Index of a drug, the greater the margin of safety.

Chloral Hydrate, a drug that has been used as a sedative for over a century, when compared to a drug in the benzodiazepine class (Diazepam - early 1960s), is an example of the lower degree

**Other Notes or Questions to Ask:**
of safety as demonstrated by drugs of the past. One of the attributes that make newer classes of drugs safer than those in the past is their ability to more selectively depress areas of the central nervous system that affect consciousness. Most anxiolytic and sedative agents, if given in inappropriate doses, have the capacity to elicit undesired effects, including coma and death.

**Chlordiazepoxide** (1957) was the first drug in the benzodiazepine class to be synthesized. The benzodiazepines, being more selective in their effects on the central nervous system, are much less likely to induce coma and death; therefore they have a much higher LD50 and Therapeutic Index than drugs in other anxiolytic/sedative classes.

**The “Ideal” Oral Agent should have the following properties:**

- ✔ Fast onset
- ✔ No adverse effects – large margin of safety (respiratory, cardiovascular, others)
- ✔ “Short” acting (for office use)
- ✔ Anxiolytic with some amnesic properties
- ✔ Reversal agent available


**Benzodiazepines meet these requirements and have the following properties:**

- ✔ Sedative-Hypnotic
- ✔ Muscle Relaxant
- ✔ Anxiolytic
- ✔ Anticonvulsant
- ✔ Antidepressant
- ✔ Anterograde Amnesia


**Other Notes or Questions to Ask:**
Medications for Oral Conscious Sedation

The family of medications most commonly used for oral conscious sedation is the benzodiazepines. They were first introduced in the early 1960’s, and are among the most widely prescribed drugs in the world. Like members of your own family they are closely related and share very similar properties due to a common mechanism of action on the gamma amino butyric acid (GABA) receptors in the brain.

These GABA receptors are the neuroreceptors responsible for levels of alertness, so the shared pharmacological property of this family of drugs denotes them as sedatives or hypnotics: they cause relaxation, can induce sleep and may even allow for post-hypnotic suggestions. The interaction of the benzodiazepines at the GABA molecule occurs in the limbic, thalamic and hypothalamic levels of the CNS. Specific high-affinity benzodiazepine receptors have been identified. When the benzodiazepine and GABA molecules interact, a macromolecular complex is formed. The complex results in an influx of chloride ions as the chloride ionophore channel in the nerve axon increases in diameter, causing hyperpolarization, and an associated new resting membrane potential.

To further the familial analogy, these medications still maintain their own uniqueness despite their underlying similarity. Each medication may or may not have active metabolites, such as diazepam (Valium), and their individual plasma half-lives and mean peak concentrations vary among agents, which gives rise to different medication properties. It is only through experience that practitioners learn how to match the best medication and dose with each clinical situation and patient.

Other Notes or Questions to Ask:
The Benzodiazepine Family of Medications

All of the benzodiazepine drugs have a similar chemical structure:

**Diazepam (Valium)**
- Produces mild sleep and mild amnesia
- Onset: 30-60 minutes
- Half-Life: 50 hours (20-100) due to active metabolites
- Duration of action can be 6-8 hours
- Supplied in 2, 5, and 10 mg tablets
- Usual Dosage is 2-40 mg
- FDA approved anxiolytic
- High Lipid Solubility

Indications for use of diazepam as listed in the Physicians’ Desk Reference (PDR):
- Preoperative anxiolytic
- Night-time sleep (hypnotic)
- Anticonvulsant

**Benzodiazepines**

THE BLOOD-BRAIN BARRIER

A complex group of blood-brain barrier mechanisms closely controls both the kinds of substances which enter the extra-cellular space of the brain and the rate at which they enter. This mechanism is not a true “barrier” but acts like a selective gatekeeper, and comprises both anatomical structures and physiological transport systems which handle different classes of substances in different ways. The blood-brain barrier mechanisms precisely regulate the chemical composition of the extra-cellular space of the brain and prevent harmful substances from reaching neural tissue, and gives rise to a second and third compartment model for the benzodiazepines.

Other Notes or Questions to Ask:
**Lorazepam (Ativan)**
- Produces mild/moderate sleep with moderate amnesia
- Onset: 60-120 minutes
- Half-Life: 10-20 hours
- No active metabolites
- Duration: 6-8 hours
- Supplied in 0.5, 1, and 2 mg tablets
- Dosage: 2-6 mg
- Moderate Lipid Solubility

Indications for use of lorazepam as listed in the Physicians' Desk Reference (PDR):
- Preoperative anxiolytic
- Night-time sleep (hypnotic)
- Anticonvulsant

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**Triazolam (Halcion)**
- No active metabolites
- Plasma half-life is 1.5 – 2.5 hours
- Wide effective dose range
- Mean peak concentration is achieved at 1.3 hours
- Has anticonvulsant properties – can be used with the epileptic patient
- May act as a respiratory depressant at very high doses (greater than 2mg)
- Relaxation for adequate pain control – important for hard to numb patients
- Does not cause nausea (unlike nitrous oxide)
- *LD$_{50}$* is 5 grams per kilogram in rats (very safe)*

Respiratory depression represents the principal negative that is introduced with conscious sedation and left unrecognized and untreated is the cause of the most serious complication!

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**Other Notes or Questions to Ask:**
Indications for use of triazolam as listed in the Physicians’ Desk Reference (PDR):

- Preoperative sedation
- Night-time sleep
- Onset: 1 hour
- Peak effect: 1.3 hours
- Duration: 2-3 hours

Dosage (PDR):
- Adult: 0.5 mg Healthy adult
- Elderly or debilitated 0.125 mg
- Always use the lowest effective dose
- Child: Safety and efficacy not tested for patients below the age of 18

Midazolam (Versed)
- Produces moderate sleep and high amnesia
- Onset: 15-30 minutes
- Half-Life: 1.5 - 5 hrs.
- No active metabolites
- Duration: 1 hr.
- Supplied in 118 ml bottles, each mL contains 2mg midazolam
- Dosage: 0.25 to 0.75 mg/kg in children >6 months (relative maximum at 10 mg)
- High Lipid Solubility
- Not an FDA approved anxiolytic

Indications for use of midazolam as listed in the Physicians’ Desk Reference (PDR):
- Preoperative anxiolytic
- Night-time sleep (hypnotic)
- Anticonvulsant

Some licensing bodies may consider the intranasal administration of midazolam so similar to the intravenous delivery that IV sedation certification is required. Delivering the medication intranasally requires a MAD® (Mucosal Atomization) Device.

Other Notes or Questions to Ask:
Other Medications (non-Benzodiazepines)

Zaleplon is a pyrazolopyrimidine, differing in structure from the benzodiazepines but still acting selectively at the benzodiazepine receptor. The benefits of this medication are in producing sedation without many of the other effects seen with benzodiazepines. It has modest anxiolytic, myorelaxant, and anticonvulsant properties. Significant drug interactions are uncommon, and synergy with ethanol does not occur. Patients with zaleplon overdose generally do well with supportive care alone. Overdose information for zaleplon is limited and no fatalities have been reported with ingestions of up to 100 mg. Adverse effects with therapeutic use include anterograde amnesia and transient visual hallucinations.

Zaleplon (Sonata, Starnoc)
- Produces high sleep with only mild amnesia
- Onset: 30 minutes
- Half-Life: 1-2 hours
- No active metabolites
- Duration: up to 6 hours
- Supplied in 5 and 10 mg capsules
- Dosage: 10 mg (start at 5 mg in the elderly or patients with liver disease)
- Overdosage can be treated with flumazenil
- Not an FDA approved anxiolytic (approved for treatment of insomnia in adults only)

Cautions:
- hypersensitivity to zaleplon products
- depressed patients
- elderly or debilitated patients
- hepatic or severe renal impairment
- compromised respiratory condition
- concurrent use of alcohol
- tartrazine sensitivity
- Coadministration with the following medications can affect metabolism: cimetidine, digoxin, and rifampin (diphenhydramine may augment zaleplon's effects)
- Pregnancy: risk category C


Other Notes or Questions to Ask:
<table>
<thead>
<tr>
<th>Drug</th>
<th>Lipid Solubility</th>
<th>Onset (mins)</th>
<th>T₁/₂ (hrs)</th>
<th>Site of Metabolism</th>
<th>Active Metabolite</th>
<th>Working Time (hrs)</th>
<th>Usual Dosing</th>
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<td>High</td>
<td>30-60</td>
<td>&gt;24</td>
<td>CYP 1A2, 2C8, 2C19, 3A3-4</td>
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<td>10-20</td>
<td>Hepatic glucuronidation</td>
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<td>2-(6) mg</td>
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<td>1.5-2.5</td>
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<td>1.5-5</td>
<td>CYP 3A3-5</td>
<td>No</td>
<td>1</td>
<td>0.25-0.75 mg/kg</td>
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<tr>
<td>Zaleplon</td>
<td>Moderate</td>
<td>30</td>
<td>1-2</td>
<td>Aldehyde oxidase, CYP 3A4</td>
<td>No</td>
<td>1</td>
<td>10-20 mg</td>
</tr>
</tbody>
</table>

Triazolam is a near ideal sedative agent due to its pharmacological properties, which make it not only highly effective for dental sedation purposes, but it also comes with a high margin of safety.

**Triazolam: Cautions and Contraindications** (Nearly all of these cautions and contraindications apply to all benzodiazepines):

**Absolute Contraindications**
- ✔ Known hypersensitivity
- ✔ Pregnancy – benzodiazepines are known teratogens (esp. 1st trimester)
- ✔ Lack of Knowledge
- ✔ Inability to resuscitate
- ✔ Concurrent with CYP3A4 inhibitors: grapefruit juice, ketoconazole, itraconazole, nefazodone, cimetidine, and macrolide antibiotics

**Relative Contraindications**
(Risk benefit should be considered when the following medical conditions exist)
- o Alcohol intoxication – additive CNS
- o Glaucoma
- o Drug abuse or dependence
- o Pediatric patients
- o Elderly (oversedation, dizziness, or impaired coordination)
- o Psychiatric patients
- o Renal impairment
- o Severe hepatic impairment
- o Lactating patients

**Other Notes or Questions to Ask:**
“Triazolam is chemically related to diazepam and is used for the short-term treatment of insomnia. Its rapid onset, short duration of action, and lack of active metabolites also makes it a near ideal anti-anxiety medication for dental patients”.


**Benzodiazepine Reversal Agent**

**Flumazenil** (Romazicon® in U.S., Anexate® in Canada):

- First clinical trials done in 1979
- Displaces BDZ's from their receptor site, reversing their sedative action
- Onset of reversal after I.V. injections is 1-2 minutes (neutral ligand)
- Duration of effect depends on the dose of flumazenil and the dose of the BDZ
- Adult dose is 0.2mg q1min up to 5 doses

Flumazenil, a nonspecific competitive antagonist of the benzodiazepine receptor, is used for reversal of benzodiazepine-induced sedation, and overdose. It binds to GABA-receptor sites, but has no agonist activity.

*** It is not recommended for routine reversal as seizures and cardiac dysrhythmias can occur with flumazenil administration, and although the majority of these effects are uncommon and well tolerated. Co-ingestion of drugs with proconvulsant properties is associated with an increased risk of seizures, presumably due to loss of the benzodiazepine’s protective anticonvulsant effect when the antagonist is administered. Combined overdose of benzodiazepines with tricyclic antidepressants accounts for 50% of these seizures. Coingestants possessing prodysrhythmic properties, such as carbamazepine or chloral hydrate, may increase the likelihood of cardiac effects by a similar mechanism.

*** Although flumazenil reverses benzodiazepine-induced sedation, it does not consistently reverse respiratory depression. The initial adult dose of flumazenil is 0.2 mg given intravenously over 30 seconds. A second dose of 0.2 mg may be given, followed by 0.2mg

**Other Notes or Questions to Ask:**
doses at 45-60 second intervals, to a total of 1mg in twenty minutes. Most patients will respond to less than 1 mg.

*** In children, the initial dose is 0.01 mg/kg.

*** Because the duration of action of flumazenil is short (40-80 minutes), resedation occurs in up to 65% of patients and requires either redosing or continuous infusion (0.25 to 1.0 mg/hr).

**In summary, flumazenil should be used for selected patients with significant symptoms from a known benzodiazepine overdose, and not routinely used on patients following an oral sedation procedure.**

Flumazenil -- Other points to note are:

1. Insoluble in water
2. Slightly soluble in acidic solutions
3. Dilute concentration of 0.1mg/mL
4. 5 mL and 10 mL vials
5. One hour duration (triazolam’s half-life is about 2 hours so patients could re-sedate)
6. Can be given sublingual in the canine to first molar area, 2-3 mm under the mucosa, not in the midline
7. Buy the 5mL vials and be aware of expiry dates!

Contraindications:
- Known hypersensitivity to benzodiazepines
- Patients with known seizure disorders treated with a benzodiazepine

Several studies support the use of flumazenil in the treatment of benzodiazepine overdose. :

✓ “Respiratory depression mediated by benzodiazepines can be reversed using the specific antagonist flumazenil (Romazicon). It can be titrated intravenously or injected sublingually in 0.2 mg increments every 2-3 minutes, up to 1 mg. Flumazenil should not be administered to patients with a history of seizure disorder or dependence on benzodiazepines.”

✓ “Clinical trials using flumazenil to reverse the CNS depression associated with intravenous diazepam sedation for third molar extractions have demonstrated its efficacy.”

**Other Notes or Questions to Ask:**
Some Definitions

- **Synergism:** When two or more drugs with similar pharmacologic effects act together to produce a greater effect than either drug alone. Synergism can either be additive or potentiating.
  
  o **Additive:** The combined drug effects are essentially the algebraic sum of their individual effects (e.g., $1 + 1 = 2$).

  o **Potentiating:** The combined drug effects are greater than the sum of their individual effects (e.g., $1 + 1 > 2$).

### Antihistamines

There are several other drugs that are effective for oral sedation, but don’t fall into the previous drug classes that have been discussed. The H1-receptor antagonist hydroxyzine (Atarax) has both sedative and hypnotic properties. The OTC antihistamine diphenhydramine (Benedryl) have hypnotic properties and can be an inexpensive and safe adjunct to sedation. Both Atarax and Benadryl are useful in allergic rhinitis and urticaria, and are antiemetic.

#### Hydroxyzine (Atarax or Vistaril)

- Diphenylmethane, unrelated to benzodiazepines, phenothiazines, or opiates
- H1-receptor antagonist
- Bronchodilator
- Antisialogogue (anticholinergic)
- Antiarrhythmic
- Anxiolytic
- Even at high doses produces minimal CV and respiratory depression
- High therapeutic index
- Produces moderate sleep with no amnesia

#### Other Notes or Questions to Ask:
Antihistaminic, Decongestant, and Anti-emetic actions

- Onset: 1 hour
- Half-Life: 3-7 hours
- No active metabolites
- Duration: 3-6 hours
- Supplied in 10, 25, and 100 mg tablets and a 10mg/5mL syrup
- Dosage: Adults 50-100 mg, Children 10-50 mg
- Overdosage: No specific antidote
- FDA approved anxiolytic and as a pre- and postoperative adjunctive medication

Contraindications:
- Early Pregnancy
- Known Hypersensitivity
- Nursing Mothers
- Children <1 year
- Acute narrow angle glaucoma
- Use with other CNS depressants cautiously

Phenergan is from the phenothiazine class but has H1-receptor effects. It has strong antihistamine properties and is commonly used in conjunction with opioid anesthesia, due to its antiemetic properties. Phenergan’s antiemetic protection is primarily due to its interaction with dopaminergic receptors in the CTZ (Chemotactic Trigger Zone).

Some important points about Phenergan:
- Will not produce unconsciousness, and even at higher doses will not cause respiratory or CV depression
- Sedative
- Antisialagogue (Anticholinergic effects)
- Strong antiemetic

Nitrous Oxide

“I am sure the air in heaven must be this wonder working gas of delight”
- Robert Southey, about Nitrous Oxide

Historical Perspective

The discovery of nitrous oxide (and also oxygen) is credited to Joseph Priestley in 1793. During experiments with iron filings, ammonium nitrate, and water, he found that a residual gas was given off which later became known as nitrous oxide.

Other Notes or Questions to Ask:
NH₄NO₃ + H₂O + Fe → N₂O + Fe(OH)₂ + H₂O

Ammonium nitrate is heated in the presence of iron filings. The resultant gas is then passed through water to remove toxic by-products. The result is nitrous oxide.

The first person to inhale pure nitrous oxide was Humphrey Davy (at the Pneumatic Institute in Bristol, England), in 1798. At that time, nitrous oxide (N₂O) was thought to be responsible for many diseases, however after breathing the gas he reported a euphoric feeling, and “overwhelming joy.”

For the first half of the 19th century, the analgesic properties of N₂O went unnoticed and nitrous was widely used as a recreational drug. It was not until the mid-1840’s that a dentist named Horace Wells while attending a demonstration was exposed to N₂O. During this demonstration a man named Samuel Cooley, after inhaling the gas, injured his leg. Dr. Wells noticed that Mr. Cooley appeared to be unaware of the injury to his leg, and he instantly envisioned the gas as an adjunct to the field of dentistry. Horace Wells in fact became the first person to have a tooth extracted while under N₂O anesthesia. He termed this revelation the “greatest discovery ever made,” and tried over the next year to prove the efficacy of N₂O to the medical community. After a failed experiment at Harvard Medical School in 1845 in which the patients “felt some discomfort,” Wells was labeled as a “charlatan” and a “fake.” He died some years later, never receiving the credits for his discovery.

Nitrous oxide lost favor and was very seldom used outside of dentistry until the 1930’s. It was then that medical schools began teaching the techniques of N₂O sedation. From that time until the late 1950’s, the medical field predominately used N₂O as a preanesthetic gas for Halothane. Dental schools began teaching inhalation anesthesia in the early 1960’s and it is estimated that “56% of GP’s and 85% of oral surgeons” use N₂O in their practice today.

**Advantages of Combination Oral-Inhalation Sedation**

- Decreased dose required of either medication alone
- Decreased overall side effects
- Potentiation vs Synergy

**Other Notes or Questions to Ask:**
<table>
<thead>
<tr>
<th>Drug</th>
<th>Tmax (hr)</th>
<th>T&lt;sub&gt;1/2&lt;/sub&gt; elim (hr)</th>
<th>Site of metabolism</th>
<th>Pharmacologic antagonist</th>
<th>Usual PO dose</th>
<th>Duration of action (hr)</th>
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<tbody>
<tr>
<td>Triazolam</td>
<td>1.25</td>
<td>2.5 (1.7-4)</td>
<td>CYP 3A4, 5-7</td>
<td>Flumazenil</td>
<td>0.125-0.5 mg</td>
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<tr>
<td>Midazolam</td>
<td>0.5-1</td>
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<td>0.5 mg/kg</td>
<td>1-2</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>1.2</td>
<td>15.7 (14-16)</td>
<td>Hepatic gluronidation</td>
<td>Flumazenil</td>
<td>1-3 mg</td>
<td>6-8</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>1.45</td>
<td>14.5 (12-15)</td>
<td>CYP 3A4</td>
<td>Flumazenil</td>
<td>1 mg</td>
<td>6-8</td>
</tr>
<tr>
<td>Diazepam</td>
<td>1.12</td>
<td>33 (20-100)</td>
<td>CYP 1A2, 2C8, 2C19, 3A3-4</td>
<td>Flumazenil</td>
<td>5-10 mg</td>
<td>6-8</td>
</tr>
<tr>
<td>Zaleplon</td>
<td>0.5-1.5</td>
<td>1</td>
<td>Aldehyde oxidase, CYP 3A4</td>
<td>Flumazenil</td>
<td>10 mg</td>
<td>4</td>
</tr>
<tr>
<td>Zolpidem</td>
<td>1.6</td>
<td>2.5</td>
<td>CYP 3A4, 2C9, 1A2</td>
<td>Flumazenil</td>
<td>10 mg</td>
<td>8</td>
</tr>
<tr>
<td>Ramelteon</td>
<td>0.3</td>
<td>0.5-2.6</td>
<td>CYP 1A2, 2C, 3A4</td>
<td>Unknown</td>
<td>8 mg</td>
<td>24</td>
</tr>
<tr>
<td>Eszopiclone</td>
<td>1-1.5</td>
<td>6</td>
<td>CYP 3A4, 2E1</td>
<td>Flumazenil</td>
<td>2-3 mg</td>
<td>6</td>
</tr>
<tr>
<td>Zopiclone</td>
<td>1-1.5</td>
<td>3.5-6.5</td>
<td>CYP 3A4, 2E1</td>
<td>Flumazenil</td>
<td>7.5 mg</td>
<td>&lt; 24</td>
</tr>
<tr>
<td>Promethazine</td>
<td>2-3</td>
<td>7-15</td>
<td>CYP 2D6, 2B6</td>
<td>None</td>
<td>25 mg</td>
<td>2-8</td>
</tr>
<tr>
<td>Hydroxyzine</td>
<td>2.1</td>
<td>7-20</td>
<td>CYP 2D6</td>
<td>None</td>
<td>50 mg</td>
<td>24</td>
</tr>
</tbody>
</table>
Physiologic Monitoring For Adult Enteral Sedation


Source: American Society of Anesthesiology (www.asahq.org)

Other Notes or Questions to Ask:
Monitoring: “In office conscious sedation mortality & serious morbidity are exceedingly rare in modern practice.”
~ Dr. John Yagiela

Blood Pressure:
- Systolic Blood Pressure (SBP)
  Reflects peak pressure in vascular system
- Diastolic Blood Pressure (DBP)
  Reflects resting pressure in vascular system
- Mean Arterial Pressure (MAP)
  Reflects average pressure in vascular system
  \[
  MAP = \frac{SBP + (2 \times DBP)}{3}
  \]

Heart Rate:
- Normal   60-100 bpm
- Bradycardia <60 bpm
- Tachycardia >100 bpm

On November 21, 2017 the American College of Cardiology and American Heart Association introduced new blood pressure guidelines...

2017 Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults

### BP Classification (JNC 7 and ACC/AHA Guidelines)

<table>
<thead>
<tr>
<th>SBP</th>
<th>DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;120 and &lt;80</td>
<td></td>
</tr>
<tr>
<td>120–129 and &lt;80</td>
<td></td>
</tr>
<tr>
<td>130–139 or 80–89</td>
<td></td>
</tr>
<tr>
<td>140–159 or 90–99</td>
<td></td>
</tr>
<tr>
<td>≥160 or ≥100</td>
<td></td>
</tr>
</tbody>
</table>

- Normal BP
- Prehypertension
- Stage 1 hypertension
- Stage 2 hypertension
- Elevated BP
- Stage 1 hypertension
- Stage 2 hypertension
- Stage 2 hypertension

- Blood Pressure should be based on an average of ≥2 careful readings on ≥2 occasions
- Adults being treated with antihypertensive medication designated as having hypertension

Other Notes or Questions to Ask:
Definitions:

Ventilation – refers to carbon dioxide elimination and is monitored by a stethoscope and/or end-tidal CO₂

Oxygenation – refers to O₂ being delivered to cells and is monitored by a pulse oximeter

Respiration

Monitoring the respiratory status of the patient is vitally important for sedation patients!

During sedation, changes in breathing are often noted well before cardiovascular changes

Respiration may be monitored by:

1) Determining the respiratory rate
2) Observing rise and fall of the chest wall
3) Observing the color of mucous membranes
4) Observing inflation and deflation of the reservoir bag if inhalation sedation is used

Visualization of inflation/deflation of the reservoir bag is a valid method of determining air exchange if an airtight seal of the mask is maintained

Holding a mirror or an ungloved hand in front of the patient’s mouth or nose so that air is felt (or seen fogging the mirror) is a good method of determining exchange of air is occurring

Respiration - devices used to assess respiration include:

- Precordial stethoscope
- Pretracheal stethoscope
- Esophageal stethoscope

A precordial / pretracheal stethoscope involves a weighted stethoscope head secured in place with tape to either the precordial or pretracheal area

The esophageal stethoscope is designed for placement into the patient’s esophagus through their nose or mouth

- This obviously would not be tolerated during oral sedation, but is excellent for general anesthesia

Other Notes or Questions to Ask:
Pulse Oximeter

- PaO\textsubscript{2} = partial atmospheric pressure of oxygen that is dissolved in the blood. Measured in mmHg
- SaO\textsubscript{2} = oxygen saturation of the blood as defined as % of heme sites occupied by an oxygen molecule
- SpO\textsubscript{2} = estimate of oxygen saturation as calculated by the pulse oximeter

The relationship between the amount of oxygen dissolved in the blood and the amount attached to the hemoglobin is called the oxyhemoglobin dissociation curve

- 97% saturation = 97 mmHg (PaO\textsubscript{2}) $\rightarrow$ Normal
- 90% saturation = 60 mmHg (PaO\textsubscript{2}) $\rightarrow$ Danger!
- 80% saturation = 45 mmHg (PaO\textsubscript{2}) $\rightarrow$ Severe Hypoxia!

Other Notes or Questions to Ask:
Oxyhemoglobin Dissociation

Changes in this curve can be caused by:
1. Alkalosis/Acidosis
2. Changes in PaCO₂
3. Hypothermia/Hyperthermia
4. Increased or decreased 2-3-DPG (a normal by-product of red blood cell metabolism)

Considerations for Pulse Oximetry:
- Effect of non-functioning hemoglobin:
- Pulse ox only measures oxygenated hemoglobin (HbO₂) and deoxygenated hemoglobin (Hb)
- When patients have large amounts of non-functioning hemoglobin pulse oximeter readings can vary widely!
  - Carboxyhemoglobin (HbCO)
  - Methemoglobin (METHb)

Other Notes or Questions to Ask:
Anemia (a lack of red blood cells causes anemia)

↓ Hemoglobin

The small of amount of hemoglobin may be well saturated with oxygen

Pulse ox readings will be normal

Changes in pulse ox are concerning b/c pt may not have enough O₂ going to tissues

Dyes

Some surgical dyes can impact Pulse Ox use

Dyes can alter light transmission thru blood

If the patient’s blood contains the following dyes, pulse oximetry cannot be used:

- Methylene blue
- Indocyanine green
- Indocarmine

Bilirubin, the breakdown product of RBC, does not affect Pulse Ox readings

Common sources of error:

- Light interference – consider covering the site
- Movement artifacts – usually pulse readings
- Sensor application – tight vs. loose
- Inadequate blood flow – BP cuff, tight clothing
- Nail polish

What else is out there for patient assessment during in-office sedation?

Bispectral Index Monitoring (BIS)

BIS Monitoring measures EEG on a dimensionless scale from 0-100. A BIS reading of 0 corresponds to flat-line EEG (no brain activity). A BIS of 95 to 100 is normal. A BIS reading of ≤ 60 is commonly considered general anesthesia.

Other Notes or Questions to Ask:
What about Pulse CO-Oximetry?

Pulse CO-Oximeter measures:
1. Pulse
2. Oxygen saturation
3. Carboxyhemoglobin
4. Methemoglobin

Remember that pulse oximeters show oxygen saturation as SpO₂ (an estimate of the true oxygen saturation)

“True” oxygen saturation is written as SaO₂

In the blood, carbon monoxide combines with hemoglobin to form carboxyhemoglobin (COHb)

In smokers, the amount of COHb in the blood ranges from 5-15%.

In non-smokers the level is 0.3-1.6%
Even in places of environmental pollution the level does not exceed 1.9%
Affinity of carbon monoxide for hemoglobin is 200x that of oxygen

High levels of carboxyhemoglobin causes a left shift in the oxyhemoglobin dissociation curve – more difficult for tissues to extract oxygen. Result is chronic tissue hypoxia – body compensates with more RBC

Net effect = increased oxygen availability at the expense of plasma viscosity

Currently pulse oximeters can only measure oxyhemoglobin (HbO₂) and deoxyhemoglobin (HHb); COHb can not be measured.

The pulse oximeter will grossly overestimate the oxygen saturation in chronic smokers!

For every 1% of circulating carboxyhemoglobin, the pulse oximeter over reads by 1%. Fifty percent of cigarette smokers have a carboxyhemoglobin concentration of 6%.⁵

Source: Anesthesia Progress 2000;47:143-150

Pulse oximeter will show HbO₂ + COHb (normal pulse oximeters can not differentiate the two hemoglobin species)

Example: Pulse oximeter reads 99% on a chronic smoker. If they have 10% COHb then the true reading of HbO₂ is 89%!!!

Other Notes or Questions to Ask:
How do Pulse Oximeters calculate SpO₂?

\[
\text{Fractional SpO}_2 = \frac{O_2\text{Hb} \times 100\%}{O_2\text{Hb} + \text{Hb} + \text{COHb} + \text{MetHb}}
\]

Clinically...\(\text{SpO}_2 = O_2\text{Hb} - \text{COHb}\)

What is Methemoglobinemia?

- Can occur in patients given extremely large doses of Prilocaine (>8 mg/kg or >8 carps in a 70 kg adult)
- The metabolite of Prilocaine, \(o\)-toludine, causes oxidation of the iron atom in hemoglobin from the reduced to the oxidized state. \(\text{Fe}^{2+} \rightarrow \text{Fe}^{3+}\)

Medications associated with Methemoglobinemia:

- Local Anesthetics (Prilocaine, Benzocaine)
- Analgesics (Acetaminophen, Celecoxib)
- Antibiotics (Sulfonamides)

Methemoglobinemia:

- The resultant species of hemoglobin - Methemoglobin is unable to transport oxygen
- Patient appears cyanotic
- Blood takes on a bluish hue

*Fortunately, for most patients methemoglobinemia is well-tolerated*

Of concern are pediatric patients, patients with cardiovascular or pulmonary disease, or patients with hereditary methemoglobinemia

Other Notes or Questions to Ask:
For compromised patients or patients with hereditary methemoglobinemia, **Prilocaine & Benzocaine should be avoided**

Treatment of Methemoglobinemia = IV methylene blue

Organs with high oxygen demands (ie CNS, cardiovascular) usually are the first systems to manifest toxicity

Normal methemoglobin fraction = 1%
- At 3-15% signs may include changes in skin color
- At 15-20% patients may be relatively asymptomatic, but cyanosis is likely present
- At 25-50%, the signs and symptoms are:
  - Headache
  - Dyspnea
  - Lightheadedness
  - Weakness
  - Confusion
  - Palpitations, Chest pains
  - Methemoglobinemia
- At 50-70%, the signs and symptoms are:
  - Altered mental status
  - Delirium
- Death occurs when methemoglobin fractions approach 70%

**Drugs that can cause Methemoglobinemia:**

<table>
<thead>
<tr>
<th>Medical Group</th>
<th>Rarely</th>
<th>Uncommon</th>
<th>Common</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analgesic - Antipyretics</td>
<td>Acetaminophen</td>
<td></td>
<td>Phenazopyridine</td>
</tr>
<tr>
<td></td>
<td>Fentanyl</td>
<td></td>
<td>Phenacetin</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>Phenobarbital</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-Infectives Agents</td>
<td>Chloroquine</td>
<td>Sulfonamides</td>
<td>Dapsone</td>
</tr>
<tr>
<td></td>
<td>Nitrofurantoin</td>
<td></td>
<td>Primaquine</td>
</tr>
<tr>
<td>Local or Topical Anaesthetic</td>
<td>Lidoceaine</td>
<td>Amethocaine</td>
<td>Benzocain (Topical)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cetacaine</td>
<td>Prilocaine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tetracaine</td>
<td></td>
</tr>
<tr>
<td>Vasodilators Agents</td>
<td>Nitrates</td>
<td></td>
<td>Nitrites Derivatives</td>
</tr>
<tr>
<td></td>
<td>Derivatives</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Methylene Blue</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metoclopramide</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Other Notes or Questions to Ask:**
**End-Tidal CO₂ Monitoring (ET CO₂)**
The ability to measure a patient’s exhaled carbon dioxide (CO₂)

**Advantages**
- Measures ventilation via detecting exhaled CO₂
- Rate
- Alarm

**Disadvantages**
- Non-intubated patient – difficult and inaccurate if patient is a mouth breather
- Expensive

**Capnography:**
Refers to the comprehensive measurement & display of CO₂, including end-tidal, inspired, and the capnogram (real time CO₂ waveform)

**Capnometry:**
Refers to the measurement and display of CO₂ in numeric form only
Normal PaCO₂ = 40 ± 5 mmHg

ET CO₂ = 0 mmHg indicates the patient is not being ventilated
- Upper airway obstruction
- Apnea
- ET misplaced
- Ventilator disconnect / malfunction
- Disconnect of sample line
**Minimal Oral Sedation Protocols**

**Minimal Sedation** (previously known as anxiolysis) - a minimally depressed level of consciousness, produced by a pharmacological method, that retains the patient's ability to independently and continuously maintain an airway and respond normally to tactile stimulation and verbal command. Although cognitive function and coordination may be modestly impaired, ventilatory and cardiovascular functions are unaffected. (Source: ADA Sedation & General Anesthesia Guidelines, 2016)

*Anxiolysis = the elimination or diminution of anxiety*

**Medications**
- Diazepam - Valium
- Zaleplon - Sonata
- Triazolam - Halcion
- Hydroxyzine - Atarax or Vistaril
- Lorazepam - Ativan
- Alprazolam - Xanax
- Nitrous Oxide - Laughing Gas
- Ramelteon - Rozerem

The same sedative drug given in different doses can cause different responses. In the case of benzodiazepines, a small dose will cause anxiolysis/MOS, while larger doses may cause sedation or deeper levels.

**Other Notes or Questions to Ask:**
Pre-Sedation Checklist:

- Medical history reviewed (including past anesthesia history)
- Complete Airway Evaluation (eg, Mallampati score)
  Difficult Airway Patients (and the ability to rescue – open the airway)
  - Previous difficult airway
  - Obesity (BMI > 30)
  - Retrognathia, micrognathia
  - Severe Rheumatoid Arthritis (TMJ, cricoarytenoid joint)
  - Obstructive Sleep Apnea
  - Uncontrolled diabetics (with “Prayer Sign”)

**Mallampati Classifications**

- **Class 1:** Entire uvula vestibule, as well as hard palate, soft palate, and tonsillar pillars are visible
- **Class 2:** Only part of the uvula and part of the tonsillar pillars are visible
- **Class 3:** Uvula invisible, but soft palate and hard palate remain visible
- **Class 4:** Soft palate invisible, only hard palate remains visible

- This test is performed with the patient in the **sitting position**, the head held in a neutral position, the mouth wide open, and the tongue protruding to the maximum
- If the patient arches his or her tongue, the uvula is falsely obscured
- A **class I view** suggests ease of intubation and correlates with a laryngoscopic view grade I (99 to 100% of the time)
- **Class IV view** suggests a poor laryngoscopic view, grade III or IV 100% of the time

**Other Notes or Questions to Ask:**

__________________________________________________________________________
Pre-Sedation Checklist (continued)

☑ All potential drug interactions researched
  o When assessing potential drug interactions for oral sedation the two main types of interactions are: 1) Additive CNS depression, and; 2) Cytochrome p450 inhibition/induction
  o In addition to prescribed medications, interactions with herbals and nutritional supplements should be also considered

☑ All drug allergies or intolerances noted

☑ Baseline vitals taken

☑ Pre-operative instructions reviewed with the patient

☑ Dietary, habit, or medicine restrictions reviewed with the patient

☑ Informed consent given and signed

☑ Responsible companion identified for transportation to/from the appointment

☑ Post-operative condition is described
  o When to resume normal activity
  o When to resume eating/hydration
  o Pain management

☑ How to recognize a problem and when/how to contact the office

Early published directions for triazolam dental sedation...
(CDAJ 1988;54(7):511-4.)

1. The drug should be given one hour before the procedure begins
2. The drug should be administered with a small amount of water on a stomach that has been empty for at least 4 hours
3. As fear “slows” gastric emptying, it is often advantageous to administer a “night before” dose, and then treat the patient in the morning, following a restful sleep. In this case, the patient should be driven to the office for the treatment appointment.
4. Following treatment, the patient should be escorted from the office by a responsible adult companion and cautioned against operating a vehicle or similar activities for the remainder of the day.
5. Do not combine triazolam with other CNS depressants, especially ethanol
6. The drug, ideally, should be administered in the dental office with the patient being placed under observation in a recovery-type facility

According to the authors, “Doses should be individualized on the basis of age, size, anxiety, and medical history.”

Other Notes or Questions to Ask:

________________________________________________________________
________________________________________________________________
________________________________________________________________
### ASA Classification

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Normal Healthy patient</td>
</tr>
<tr>
<td>II</td>
<td>Patient with mild systemic disease</td>
</tr>
<tr>
<td>III</td>
<td>Patient with severe systemic disease that limits activity but is not incapacitating</td>
</tr>
<tr>
<td>IV</td>
<td>Patient with severe systemic disease that is a constant threat to life.</td>
</tr>
<tr>
<td>V</td>
<td>Morbid pt. who is not expected to survive 24 hours with or without an operation</td>
</tr>
<tr>
<td>VI</td>
<td>A declared brain dead pt. whose organs are being removed for donor purposes</td>
</tr>
</tbody>
</table>

### American Society of Anesthesiologists (ASA) Patient Physical Status Classification

<table>
<thead>
<tr>
<th>Classification</th>
<th>Definition</th>
<th>Examples, including but not limited to:</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA I</td>
<td>A normal healthy patient</td>
<td>Healthy, non-smoking, no or minimal alcohol use</td>
</tr>
<tr>
<td>ASA II</td>
<td>A patient with mild systemic disease</td>
<td>Mild diseases only without substantive functional limitations. Examples include (but not limited to): current smoker, social alcohol drinker, pregnancy, obesity (BMI &lt; 40), well-controlled DM/HTN, mild lung disease</td>
</tr>
<tr>
<td>ASA III</td>
<td>A patient with severe systemic disease</td>
<td>Substantive functional limitations; One or more moderate to severe diseases. Examples include (but not limited to): poorly controlled DM or HTN, COPD, morbid obesity (BMI ≥ 40), active hepatitis, alcohol dependence or abuse, implanted pacemaker, moderate reduction of ejection fraction, *ESRD undergoing regularly scheduled dialysis, premature infant PCA &lt; 60 weeks, history (&gt;3 months) of MI, CVA, TIAs, or CAD/stents.</td>
</tr>
<tr>
<td>ASA IV</td>
<td>A patient with severe systemic disease that is a constant threat to life</td>
<td>Examples include (but not limited to): recent (&lt; 3 months) MI, CVA, TIAs, or CAD/stents, ongoing cardiac ischemia or severe valve dysfunction, severe reduction of ejection fraction, sepsis, DIC, ARD or *ESRD not undergoing regularly scheduled dialysis</td>
</tr>
<tr>
<td>ASA V</td>
<td>A moribund patient who is not expected to survive without the operation</td>
<td>Examples include (but not limited to): ruptured abdominal/thoracic aneurysm, massive trauma, intracranial bleed with mass effect, ischemic bowel in the face of significant cardiac pathology or multiple organ/system dysfunction</td>
</tr>
<tr>
<td>ASA VI</td>
<td>A declared brain dead patient whose organs are being removed for donor purposes</td>
<td></td>
</tr>
</tbody>
</table>

*The addition of "E" denotes Emergency surgery: (An emergency is defined as existing when delay in treatment of the patient would lead to a significant increase in the threat to life or body part)*

Source: ADA Sedation and General Anesthesia Guidelines, 2016

Other Notes or Questions to Ask:

**Table 2. Total triazolam anxiolytic dosing guidelines (in mg).**

<table>
<thead>
<tr>
<th>Weight (lb/kg)</th>
<th>18-40</th>
<th>41-64</th>
<th>65 and older</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤100/≤45</td>
<td>0.3125*</td>
<td>0.250*</td>
<td>0.1250*</td>
</tr>
<tr>
<td>110/50</td>
<td>0.3458</td>
<td>0.275</td>
<td>0.1375</td>
</tr>
<tr>
<td>120/55</td>
<td>0.3750</td>
<td>0.300</td>
<td>0.1300</td>
</tr>
<tr>
<td>130/60</td>
<td>0.4063</td>
<td>0.325</td>
<td>0.1625</td>
</tr>
<tr>
<td>140/65</td>
<td>0.4375*</td>
<td>0.350</td>
<td>0.1750</td>
</tr>
<tr>
<td>150/70</td>
<td>0.4688</td>
<td>0.375*</td>
<td>0.1875*</td>
</tr>
<tr>
<td>160/75</td>
<td>0.5000*</td>
<td>0.400</td>
<td>0.2000</td>
</tr>
<tr>
<td>170/80</td>
<td>0.5313</td>
<td>0.425</td>
<td>0.2125</td>
</tr>
<tr>
<td>180/85</td>
<td>0.5625*</td>
<td>0.450</td>
<td>0.2250</td>
</tr>
<tr>
<td>190/90</td>
<td>0.5938</td>
<td>0.475</td>
<td>0.2375</td>
</tr>
<tr>
<td>200+/95+</td>
<td>0.6250*</td>
<td>0.500*</td>
<td>0.2500*</td>
</tr>
</tbody>
</table>

*Indicates possible triazolam dosing increments, based on available tablet strength. Note: Always round down to the nearest tablet strength.

**Table 3. Total lorazepam anxiolytic dosing guidelines (in mg).**

<table>
<thead>
<tr>
<th>Weight (lb/kg)</th>
<th>18-40</th>
<th>41-64</th>
<th>65 and older</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤100/≤45</td>
<td>1.250*</td>
<td>1.0*</td>
<td>0.50*</td>
</tr>
<tr>
<td>110/50</td>
<td>1.375</td>
<td>1.1</td>
<td>0.55</td>
</tr>
<tr>
<td>120/55</td>
<td>1.500*</td>
<td>1.2</td>
<td>0.60</td>
</tr>
<tr>
<td>130/60</td>
<td>1.625</td>
<td>1.3</td>
<td>0.65</td>
</tr>
<tr>
<td>140/65</td>
<td>1.750*</td>
<td>1.4</td>
<td>0.70</td>
</tr>
<tr>
<td>150/70</td>
<td>1.875</td>
<td>1.5*</td>
<td>0.75*</td>
</tr>
<tr>
<td>160/75</td>
<td>2.000*</td>
<td>1.6</td>
<td>0.80</td>
</tr>
<tr>
<td>170/80</td>
<td>2.125</td>
<td>1.7</td>
<td>0.85</td>
</tr>
<tr>
<td>180/85</td>
<td>2.250*</td>
<td>1.8</td>
<td>0.90</td>
</tr>
<tr>
<td>190/90</td>
<td>2.375</td>
<td>1.9</td>
<td>0.95</td>
</tr>
<tr>
<td>200+/95+</td>
<td>2.500*</td>
<td>2.0*</td>
<td>1.00*</td>
</tr>
</tbody>
</table>

*Indicates possible lorazepam dosing increments, based on available tablet strength. Note: Always round down to the nearest tablet strength.
Total Anxiolytic Dose is calculated by:

- Considering age, weight, and medical status
- Three age groups
  - 18-40 (dose increased by 25% to account for ↑ metabolism)
  - 41-64
  - 65+ (dose reduced dose 50% bc of sensitivity, and ↓ metabolism)
- ASA 3 patients – reduce dose on the chart by an additional 50%
- ASA 4 patients – contraindicated
- Relative potency of triazolam to lorazepam is 4:1

Case Example 1  
triazolam

- 34 yo H female
- 160 lbs
- PMHx: Mitral valve prolapse (MVP) w/o regurgitation, verified by Echo 5 years ago
- No medications
- No known drug allergies
- Vitals: BP 110/65 mmHg, pulse 60 bpm

CORRECT DOSE_________________________

Case Example 2  
triazolam

- 42 yo AA male
- 200 lbs
- PMHx: Asthma
- Meds: Albuterol prn
- No known drug allergies
- Vitals: BP 135/85 mmHg, pulse 100 bpm

CORRECT DOSE_________________________

Other Notes or Questions to Ask:

______________________________________________________________________________
Case Example 3

triazolam

- 65 yo male
- PMHx:
  - Type 2 Diabetes Mellitus
  - BG range 215-250 mg/dL
  - HgA1C 12%
  - Meds: glimepiride 4 mg q.d.
  - No known drug allergies
  - Vitals: BP 135/82 mmHg, pulse 87 bpm, Height 6’0”, Weight 275 lbs.

CORRECT DOSE_________________________

Case Example 4

lorazepam

- 22 yo male, 160 lbs
- PMHx:
  - Inguinal hernia repair 5 years ago
  - Prolapsed mitral valve w/ regurgitation
  - Seasonal allergies
  - Meds: Fexofenadine
  - No known drug allergies
  - Vitals: BP 120/75 mmHg, pulse 90 bpm

CORRECT DOSE_________________________

Case Example 5

lorazepam

- 74 yo male, 225 lbs
- PMHx: Angina (2-3 attacks/week)
- Meds:
  - Metoprolol 200 mg bid
  - Atorvastatin 20 mg qd
  - Aspirin 81 mg qd
  - Nitroglycerin prn
  - No known drug allergies
  - Vitals: BP 129/85 mmHg, Pulse 80 bpm

CORRECT DOSE_________________________

Other Notes or Questions to Ask:
________________________________________________________________________
________________________________________________________________________
Case Example 6
lorazepam
- 21 yo female, 140 lbs
- PMHx: Recently gave birth (3 weeks ago) and breastfeeding
- Meds:
  - Multivitamins
  - Herbal diet medication
- Allergic to PCN → hives
- Vitals: BP 105/60 mmHg, Pulse 85 bpm
- SHx: Quit smoking 9 mos. ago. Before that 1 ppd x 3 years

Case Example 7
lorazepam
- 58 yo male, 215 lbs
- PMHx:
  - CABG x 4
  - MVP w/ regurgitation
  - Joint replacement (Right knee and hip)
- Meds:
  - Cyclobenzaprine 10 mg
  - Viagra prn
- Allergies:
  - PCN
  - Clindamycin (intolerance)
- Vitals: BP 150/87 mmHg, Pulse 90 bpm
- SHx: Smokes 1 cigar/day x 30 yrs

Other Notes or Questions to Ask:
**Are there other strategies?**

- A dose of medication could be given the night before the sedation
  - May help anxious patients to relax and get to sleep
  - Establishes a blood level of the medication that can be added to the next morning
  - Reduces total drug amounts
- Incremental dosing – “oral titration” (usually not allowed without conscious sedation/moderate sedation permit)

![Graph](image-url)

**What medications could be used the night before the sedation?**

- Stick with a Benzodiazepine or Hydroxyzine
- Use longer half-life drugs
- For patients who smoke, use Hydroxyzine the night before

<table>
<thead>
<tr>
<th></th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elderly/Debilitated/CNS depressants</td>
<td>Diazepam 2.5 mg</td>
</tr>
<tr>
<td>Average</td>
<td>Diazepam 5 mg</td>
</tr>
<tr>
<td>High Fear/Resistant</td>
<td>Diazepam 10 mg</td>
</tr>
</tbody>
</table>

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**Other Notes or Questions to Ask:**

________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
Incremental Oral Administration

Important Note: the below incremental administration technique, in most cases, will require an oral conscious sedation/moderate oral sedation permit to utilize. It is included in this handout for informational purposes only.

Reminder: always verify your State’s Rules and Regulations relating to in-office sedation/anesthesia before performing any sedative technique.

Table 4. Protocol for incremental oral administration

This example is for an 8 a.m. appointment when dentistry is planned to begin at 9 a.m.

Prior to appointment: The patient (Adult ASA 1 or 2) has been evaluated by the dentist preoperatively and accepted for oral sedation dentistry; prior to appointment, the patient has received a single dose of triazolam (0.25 mg; for elderly, debilitated, or patients with potential drug interactions, 0.125 mg should be dispensed).

7:00 a.m.: The patient, having gone six hours without eating, takes 0.25 mg triazolam; a responsible companion escorts the patient to the office.

8:00 a.m.: The patient arrives at the office with the companion and compliance with preoperative instructions is verified.

8:03 a.m.: The patient is seated in the operatory for the beginning of continuous physiologic monitoring; at that time, the patient’s wristwatch and glasses are removed and given to a companion.

8:06 a.m.: The patient is assessed for susceptibility to the sedative medication; additional medication may be provided sublingually.

8:35 a.m.: The patient’s sedation state is reassessed; if additional medication is necessary, the dentist should deliver it sublingually.

8:54 a.m.: Oxygen is introduced with the appropriate protocol.

8:57 a.m.: Nitrous oxide is introduced with the appropriate protocol.

9:00 a.m.: Local anesthesia is administered; at this point, nitrous oxide administration is terminated and dentistry begins.


Other Notes or Questions to Ask:
The above graph represents a rough kinetic model of an additional dose of triazolam (i.e., supplemental dosing) to maintain sedation for a longer dental appointment.

Pharmacokinetic modeling of oral triazolam

F = 44%
Dose = 0.25mg
Vd = 70 L
Kab = 1.5 h⁻¹
Kel = 0.35 h⁻¹
Number of doses = 8
Dose interval = 2hrs

The above graph is a representation of what the plasma concentration may be after multiple doses of oral triazolam. At a dose of 0.25mg given every 2 hours, the plasma concentration approaches 2.5 μg/mL. A single 0.5mg dose typically results in plasma concentrations of approximately 4.0 μg/mL.

**Other Notes or Questions to Ask:**

________________________________________________________________
________________________________________________________________
________________________________________________________________

Friday, April 19, 2019

Friday, April 19, 2019
Pre-Sedation Instructions

- NPO for 4-6 hours (clear liquids ok), exception – diabetic patients
- No CNS depressants or sedatives for 24 hours before/after (other than night-time anxiolytic prescribed by treating dentist)
  - Smokers
  - Coffee drinkers
  - Herbal diet medications (eg, Ephedra)
  - Herbal medications
    - (eg, Kava Kava, Valerian, Chamomile, Melatonin, St. John’s Wort)
  - Nutritional supplements
- No chance of pregnancy (triazolam is pregnancy factor X)
- No allergies to the sedative medications (possible, but very rare)
- Must have a responsible person to bring them to the office and take them home (no exceptions!)
- No contact lenses (anticholinergic effects → dry eyes)
- No driving for 24 hours after the sedation appointment
- Because of prolonged psychomotor impairment - No operating hazardous machinery
- No heavy lifting (balance disturbances)
- No stairs without assistance (balance disturbances)
- No important decisions (amnesia)

### American Society of Anesthesiologists Fasting Guidelines

<table>
<thead>
<tr>
<th>Ingested Material</th>
<th>Minimum Fasting Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear liquids</td>
<td>2 hours</td>
</tr>
<tr>
<td>Breast milk</td>
<td>4 hours</td>
</tr>
<tr>
<td>Infant formula</td>
<td>6 hours</td>
</tr>
<tr>
<td>Nonhuman milk</td>
<td>6 hours</td>
</tr>
<tr>
<td>Light meal</td>
<td>6 hours</td>
</tr>
<tr>
<td>Fatty meal</td>
<td>8 hours</td>
</tr>
</tbody>
</table>

Source: American Dental Association, Sedation and General Anesthesia Guidelines, 2016

Other Notes or Questions to Ask:

__________________________________________________

__________________________________________________
Reminders

- Always remember the definition of anxiolysis/minimal sedation...patient is conscious, responds to verbal commands, patent airway at all times
- Patients may respond that they are still awake ("You are an excellent patient")
- Do not treat any patient that has a questionable or complex medical history! (ASA 1 and 2; ASA 3 with possible medication consult)
- Sedation patients are NEVER left unattended
- If the reversal agent (flumazenil) is used for any reason, no additional sedative medication should be administered, and the patient should be monitored for the appropriate time (at least one hour) before discharge
  - Check State Board Rules! – reporting
- Must manually record vital signs at least 3 times in the patient record (Pre-op, start of dentistry, at discharge)
- At the end of the appointment, or when more cooperation is needed, a sugar-drink (eg, juice, Gatorade) is provided
- Document your intention! (eg, “Minimal Sedation Provided”)
- Patient must satisfy discharge criteria and be ambulatory with minimal assistant before being released
  - Orientation x3 (Time, Place, Person)
- Post-operative instructions, verbal and written, must be given to patient and companion (retained a signed copy)

Patient Dismissal

Patient readiness for discharge needs to be addressed in a simple, clear, reproducible manner that meets accepted guidelines

- Aldrete Score (Phase 1 discharge)
- Postanesthesia Discharge Scoring System (PADSS)
- Modified Postanesthesia Discharge Scoring System :
  - Vital Signs
  - Ambulation
  - Nausea / Vomiting
  - Pain
  - Surgical Bleeding

Other Notes or Questions to Ask:

________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
Aldrete Scoring System

Aldrete Scoring System
Designed for assessment of patients for Phase 1 discharge (ie, discharge from ICU or post-anesthesia care unit).

Aldrete’s score is not intended to determine home-readiness

The modified PADSS differs from its original form by not including oral intake of fluids as a criterion for discharge.

**Aldrete Scoring System**

- Activity
  - Can move voluntarily on command
  - 2 = 4 extremities
  - 1 = 2 extremities
  - 0 = 0 extremities

- Respiration
  - 2 = Can deep-breathe and cough freely
  - 1 = Dyspnea, shallow, or limited breathing
  - 0 = Apneic

- Circulation
  - Pre-operative BP (mmHg)
  - 2 = +/- 20 mmHg from baseline
  - 1 = +/- 20-50 mmHg from baseline
  - 0 = +/- 50 mmHg from baseline

- Consciousness
  - 2 = Fully awake
  - 1 = Arousable by calling
  - 0 = Not responding

- Color
  - 2 = Normal
  - 1 = Pale, dusky, blotchy
  - 0 = Cyanotic

A score of 10 is ready for discharge.

**Modified Postanesthesia Discharge Scoring System (MPADSS)**

- Vital Signs
  - 2 = Within 20% of pre-operative value
  - 1 = 20-40% of pre-operative value
  - 0 = 40% of pre-operative value

- Ambulation
  - 2 = Steady gait / no dizziness
  - 1 = With assistance
  - 0 = more dizziness

- Nausea/Vomiting
  - 2 = Minimal
  - 1 = Moderate
  - 0 = Severe

- Pain
  - 2 = Minimal
  - 1 = Moderate
  - 0 = Severe

- Surgical bleeding
  - 2 = Minimal
  - 1 = Moderate
  - 0 = Severe

The total score is 10. With patients scoring 10 considered fit for discharge home.


Patient Dismissal
- The patient is always escorted by their companion, or a team member, while walking in the office
- Team member helps companion assist (or via wheelchair/companion chair) patient into departing vehicle
- Patient is taken directly home
- Make follow-up calls to all patients that night and remind them to hydrate
- Unconditional positive regard (always be encouraging!)
- Review all post-operative instructions with the patient’s companion
- Flumazenil should not routinely be used to aid in patient dismissal (short duration and possible re-sedation)

A Second Single Dose Appointment
Adjust on the following variables:

- Pt. Good/office good = Rx remains the same
- Pt. Good/office bad = Rx adjustment by increasing or decreasing dosage appropriately
- Pt. Bad/office bad = reassess for referral (different type of sedation) or test appt. with adjustments to protocol

Some Important Caveats to Remember:

... Increased number of drugs lowers safety ...

... Respiration most likely source of anesthetic mishap ...

... Be careful not to practice beyond your Level of Training ...

Other Notes or Questions to Ask:

________________________________________________________________
________________________________________________________________
________________________________________________________________
Flumazenil (Romazicon in U.S., Anexate in Canada):

Flumazenil, a nonspecific competitive antagonist of the benzodiazepine receptor, is used for reversal of benzodiazepine-induced sedation, conscious sedation, and overdose. It binds to GABA-receptor sites, but has no agonist activity. In the emergency room it can quickly confirm a clinical diagnosis, thereby obviating the need for time-consuming and expensive interventions. In the dental office, with patients undergoing conscious sedation with benzodiazepines, it speeds return to baseline alertness in emergency situations.

It is not recommended for routine reversal as seizures and cardiac dysrhythmias can occur with flumazenil administration, and although the majority of these effects are well tolerated, fatalities have been reported. Coingestion of drugs with proconvulsant properties is associated with an increased risk of seizures, presumably due to loss of the benzodiazepine’s protective anticonvulsant effect when the antagonist is administered. Combined overdose of benzodiazepines with tricyclic antidepressants accounts for 50% of these seizures. Coingestants possessing prodysrhythmic properties, such as carbamazepine or chloral hydrate, may increase the likelihood of cardiac effects by a similar mechanism.

Because the mechanism of action is specific to the benzodiazepine receptor in the central nervous system, other medications that work via this receptor can also be reversed with this antagonist. Examples include zolpidem (Ambien), zopiclone (Imovane), eszopiclone (Lunesta) and zaleplon (Sonata, Starnoc).

Contraindications:
- Known hypersensitivity to benzodiazepines
- Patients with known seizure disorders treated with a benzodiazepine

Other Notes or Questions to Ask:
Although flumazenil reverses benzodiazepine-induced sedation, it does not consistently reverse respiratory depression. The initial adult dose of flumazenil is 0.2 mg given intravenously over 30 seconds. A second dose of 0.2 mg may be given, followed by 0.2 mg doses at 1-minute intervals, to a total of 1 mg in twenty minutes. Most patients will respond to less than 1 mg. In children, the initial dose is 0.01 mg/kg. Because the duration of action of flumazenil is short (0.7 to 1.3 hours), re-sedation occurs in up to 65% of patients and requires either re-dosing or continuous infusion (0.25 to 1.0 mg/hr).

In summary, flumazenil should be used for selected patients with significant symptoms from a known benzodiazepine overdose and not routinely used in patients with altered mental status. Other points to note are:

2. Insoluble in water
3. Slightly soluble in acidic solutions
4. Dilute concentration of 0.1 mg/mL
5. 5 mL and 10 mL vial
6. One hour duration (triazolam’s half-life is about 2 hours so patients could re-sedate)
7. Can be given sublingual in the canine to first molar area, 2-3 mm under the mucosa, not in the midline
8. Buy the 5 mL vials and be aware of expiry dates!
**Growing Body of Evidence: References with Summaries**


PURPOSE: The purpose of this study was to examine intralingual (IL) and submucosal (SM) delivery of flumazenil as viable alternatives to immediate intravenous (IV) administration for reversing benzodiazepine sedation in an animal model. METHODS: A dog animal model was chosen based upon comparable body weight to children (12-17 kg) and the ease of oral access in this species. Research design was a non-randomized matched pair study. This type of "before and-after study" allowed the dogs to receive 3 different routes of flumazenil administration (IV, IL, and SM) following an initial dose of midazolam (0.5 mg/kg IV). Blood samples were obtained (at 0, 2, 4, 8, 15, and 30 minutes) for high performance liquid chromatography (HPLC) analysis of flumazenil and midazolam, and oxygen saturation values were recorded. RESULTS: Both IL and SM delivery of flumazenil were determined to be viable alternatives to immediate IV administration for reversing benzodiazepine-induced oxygen saturation (SaO2) desaturation. For flumazenil to be able to reverse the SaO2 desaturation, the plasma levels must be greater than 5ng/ml, which was exceeded by IL and SM drug delivery. CONCLUSION: In a benzodiazepine-induced desaturation, the submucosal and intralingual routes are viable alternatives to intravenous administration of flumazenil in an animal model.


PURPOSE: This study was performed to determine the bioavailability and local tissue toxicological safety of flumazenil (Romazicon) when administered by oral submucosal (SM) as opposed to intravenous (i.v.) injection. METHODS: Six dogs each received SM flumazenil (0.2mg), and their serum was collected at predetermined time intervals (0-2 h) and frozen (-70 degrees C). Seven days later, the dogs received an identical dose of i.v. flumazenil, and serum samples were again collected, as above. Comparative quantitation of flumazenil levels (i.v. vs.SM) was made using a sensitive HPLC assay (UV detection). Direct/local drug toxicity was visually scored by unbiased raters of color photographs (test and control mucosa) taken at 1, 2, and 7 days following SM flumazenil injection. An oral pathologist examined slides processed from control and treatment tissues (hematoxylin and eosin staining) taken (punch biopsy) 1 week following SM injection to compare with direct clinical scores. RESULTS: Serum flumazenil levels reached a plateau (8.5 +/- 1.5 ng/mL, mean +/- SD) within 4 min of SM drug injection and declined thereafter to -2 ng/mL by 2 h. Bioavailability of SM flumazenil was 101 +/- 14%, based upon measuring the area under the serum concentration-time curves over 1.5 h (AUC 0-1.5 h, SM vs. i.v. drug). Thus, serum drug levels following SM drug administration were broadly comparable to those obtained during the elimination phase of corresponding i.v. drug delivery. Regarding drug tissue toxicity, no evidence of direct drug toxicity was observed by unbiased raters of color photographs (test and control mucosa) taken at 1, 2, and 7 days following SM flumazenil injection. Following pathologic review, no difference was seen in the degree of inflammation between treatment and control tissue. CONCLUSION: At the quantity and concentration used, SM drug flumazenil administration appears to be both a safe and a viable alternative to bolus i.v. drug delivery and worthy of further investigation.


OBJECTIVE: To determine whether flumazenil, a drug used to reverse benzodiazepine-induced respiratory depression and approved only for i.v. use, is effective by alternative routes. METHODS: A randomized, controlled, nonblinded, crossover canine trial was performed to evaluate reversal of midazolam-induced respiratory depression by flumazenil when administered by alternative routes. Mongrel dogs were sedated with thiopental 19 mg/kg i.v., then tracheally intubated. With the dogs spontaneously breathing, tidal...
volume, end-tidal CO2, and O2 saturation were observed until a stable baseline was achieved. Incremental doses of midazolam were administered until respiratory depression (30% decline in tidal volume, 10% decrease in O2 saturation, and 15% increase in end-tidal CO2) occurred. Flumazenil was administered by a randomly selected route [0.2 mg followed 1 minute later by 0.3 mg i.v., sublingual (s.l.) or intramuscular (i.m.); or 1 mg followed 1 minute later by 1.5 mg per rectum (PR)]. Time to return to baseline respiratory functions was recorded ("time to reversal"). Each of 10 dogs was studied using all 4 routes of flumazenil administration with a washout period of at least 7 days. An additional dog served as a control (no flumazenil).

**RESULTS:** The control time to reversal was 1,620 seconds. The i.v. route was significantly faster (mean 120 +/- 24.5 sec) than the other 3 routes (p<0.005). The SL route was the second fastest (mean 262 +/- 94.5 sec), the IM route was the third fastest (mean 310 +/- 133.7 sec) and the PR route was the slowest (mean 342 +/- 84.4 sec). The SL, IM, and PR routes did not differ significantly from one another.

**CONCLUSIONS:** Flumazenil administered by all 4 routes reversed midazolam-induced respiratory depression in a dog model. For the selected dosages used, the i.v. route was significantly faster than all 3 other routes, and SL was the second fastest.


In an open design, randomised, two-way cross-over study, a single 2 mg i.v. dose and a single 30mg oral dose of flumazenil were each administered to a group of healthy young (n = 6) and elderly (n = 12) volunteers (male: female 2/1). Plasma samples were collected at intervals and intact drug was assayed. Both the i.v. and oral doses of flumazenil were very well tolerated by both age groups and no severe or unexpected adverse effects were observed. The main complaints were dizziness and headache, mainly after oral dosing, probably due to the higher Cmax and AUC following this route of administration. After 2 mg i.v. the disposition parameters in the two age groups (elderly/young) were very similar: volume of distribution (Vss): 0.88/0.90 L/kg; total body clearance (ClPL): 0.86/0.99 L/min; terminal elimination half-life (t1/2 beta): 1.02/0.91 h. After the 30 mg oral dose the mean Cmax of 87.6 ng/mL (elderly) and 78.4 ng/mL (young) were generally reached within 0.5 to 1 h. In 26% (elderly) and 23% (young), the absolute bioavailability of flumazenil was very similar. It is concluded that the absorption and disposition parameters of flumazenil were not significantly affected by aging.


Triazolam is increasing in popularity as a premedication prescribed by dentists to help their fearful and anxious patients tolerate the potentially aversive nature of some dental procedures. Recent anecdotal reports suggest that incremental sublingual dosing of triazolam may be an effective technique for producing conscious sedation in the dental setting. Although promising, no laboratory or clinical data have been available to evaluate the efficacy or safety of this approach. This study was designed to determine the pharmacokinetics and sedative effects of incremental sublingual dosing of triazolam (total, 1.0 mg) in healthy adults. Ten healthy adult volunteers received sublingual triazolam (0.25 mg) followed by additional doses after 60 (0.50 mg) and 90 (0.25 mg) minutes. Plasma triazolam concentrations, clinical effects (Observer's Assessment of Alertness/Sedation score), and processed electroencephalogram (bispectral index score) were measured intermittently for 3 hours. Plasma triazolam concentrations (mean +/- SD, 5.1 +/- 1.1 ng/mL) and drug effects (Observer's Assessment of Alertness/Sedation score, 2 +/- 1; and the bispectral index score, 62 +/- 16) were greatest in all subjects at the end of the 3-hour evaluation period. Eight of the subjects had Observer's Assessment of Alertness/Sedation scores consistent with the definition of deep sedation or general anesthesia (Observer's Assessment of Alertness/Sedation score, <3) at some of the later time points in the 180 minutes of data collection. In comparison, 4 of the subjects had bispectral index scores less than 60 during these later time points of data collection. Given the considerable intersubject variability in triazolam concentrations and effects, additional research is needed to assess this multidosing strategy before it can be endorsed as a useful and safe sedation technique for managing fearful and anxious patients in dental practice.

**Other Notes or Questions to Ask:**
Can we make sedation even safer?

- Start with intrinsically safe medications that have the best evidence for use.
- Ensure that you and your staff are well-educated, trained and up to date with your certifications (BLS, HCPBLS, ILS, PALS, ACLS).
- Practice, practice, practice
- Monitoring will keep your patients safer too: Blood pressure, pulse, heart rate, oxygen saturation (pulse oximetry).
- Regardless, you need to know what to look for clinically, and how your monitoring equipment works.

Other Notes or Questions to Ask:
In the blood, carbon monoxide combines with hemoglobin to form carboxyhemoglobin (COHb).

In smokers, the amount of COHb in the blood ranges from 5-15%.

In non-smokers the level is 0.3-1.6%.

Affinity of carbon monoxide for hemoglobin is 200x that of oxygen.

Causes a left shift in the oxyhemoglobin dissociation curve – more difficult for tissues to extract oxygen.

Result is chronic tissue hypoxia – body compensates with more RBC:

Net effect = increased oxygen availability at the expense of plasma viscosity

Currently pulse oximeters can only measure oxyhemoglobin (HbO2) and deoxyhemoglobin (HHb); carboxyhemoglobin (COHb) is not being measured.

The pulse oximeter will grossly overestimate the oxygen saturation in chronic smokers!

Pulse oximeter shows the combination of HbO2 + COHb, not the individual components.

Example: Pulse oximeter reads 99% on a chronic smoker. If they have 10% COHb then the true reading of HbO2 is 89%!!!

New, non-invasive co-pulse oximetry measures:
- Oxyhemoglobin
- Reduced Hemoglobin
- Methemoglobin
- Carboxyhemoglobin

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Other Notes or Questions to Ask:

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Can we make sedation even safer?

- Bispectral Index System (BIS) Monitoring Video (courtesy of Aspect Technologies).
- Clinical Interpretation of Bispectral Analysis


And, of course, there will always be new drugs . . .

Ramelteon (Rozerem®)

- Approved for use by the FDA in October 2005
- First in a new drug class of melatonin receptor agonists.
- More potent than melatonin. It helps people FALL asleep, but doesn't necessarily help them STAY asleep.
- People take Rozerem 8 mg a half hour before bedtime - higher doses don't work any better.
- ONSET. Generally works within 30 minutes.
- LENGTH OF USE. Only Rozerem is NOT limited to short-term use in true insomniacs.
- DEA. Rozerem is the only anxiolytic/sedative that's NOT a controlled substance.
- COST. Less than Ambien, Sonata, or Lunesta but generics are always on the horizon.

Other Notes or Questions to Ask:
Naloxone (Narcan®) – Narcotic Antagonist

Indications:
• Reversal of narcotic depression including respiratory depression induced by opioids, (both natural and synthetic narcotics), propoxyphene, and narcotic-antagonist analgesics
• Diagnosis of suspected acute narcotic overdosage
• Not effective in counter-acting depression due to barbiturates, tranquilizers or other non-narcotic anesthetics or sedatives

Routes of Administration:
• IM, SC - when IV route not feasible; onset of action not as prompt as with IV and may be delayed in patients who are hypotensive and have impaired peripheral circulation
• IV direct - slowly over at least 1 minute


Dosage, Adults:
• Known or suspected overdose: 0.4-2 mg IV; if no response, repeat 2-4 mg in minutes; in cases of large narcotic overdoses, or methadone, pentazocine, propoxyphene overdose, higher doses may be required; if no response after 10 mg, reassess diagnosis; effective dose may be repeated every 20-60 minutes
• Post-operative respiratory depression: 0.1-0.2 mg at 2-3 minute intervals until desired response is obtained; repeat doses may be required at 1-2 hour intervals
• Partial reversal of opioid-associated respiratory depression in palliative patient: if respiratory rate < 6/minute, administer 0.1-0.2mg IV q2-3 minutes or 0.1-0.2mg SC q5-10minutes until respiratory rate > 10/minute. Continue to monitor respiratory rate q15minutes until no naloxone given x 1 hour.

Dosage, Children:
• Known or suspected overdose:
  • Birth to 5 yrs or 20 kg: 0.1 mg/kg/dose; repeat at 2-3 minute intervals until desired response obtained
  • > 5 yrs or > 20 kg: 2 mg; repeat as above
• Post-operative respiratory depression: 0.005-0.01 mg/kg IV repeated if necessary at 2-3 minutes intervals
• Onset of effect: within 1-2 minutes following IV, within 2-5 minutes following IM or SC
• Duration of effect: 45 minutes to 3-4 hours
• Since duration of action of narcotic agent may exceed that of naloxone, repeated doses or administration of naloxone via IV infusion may be required


Other Notes or Questions to Ask: