PEAK

Oral sedation in dental practice

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In the last number of years there has been increased interest in oral sedation in dentistry, from the perspectives of both the public and the profession. In part, this has arisen from a recognition that improving access to care should include helping those who have difficulty seeing a dentist because of fear or anxiety.

Whereas, many years ago, it was common to assume that any dentist could carry out oral sedation, a number of tragic outcomes (Coté et al, 2000) has led to the recognition that specific education is required in order to do this safely. The Royal College of Dental Surgeons of Ontario (RCDSO) has published a Standard of Practice for the Use of Sedation and General Anesthesia in Dental Practice, which states:

"*Successful completion of a training program designed to produce competency in the specific modality of sedation or general anaesthesia utilized is mandatory*" (RCDSO, 2012a).

This responsibility applies to oral sedation. Most dental schools do not provide training to the level of moderate sedation but often only to the level of minimal sedation, if that, normally limited to the use of a single oral sedative alone or nitrous oxide and oxygen alone. Education to the level of competence for a combination technique or moderate sedation can be obtained in general practice residencies, a number of specialty programs, and continuing education courses. There are no specific guidelines for this training in Canada, whereas in the United States, the American Dental Association does have published recommendations (ADA, 2007). The purpose of this article is to provide a synopsis of oral sedation in dentistry. It is not intended to replace appropriate training, but merely to be a supplement or a review. This article is based on an existing publication (Haas, 2011). The reader is also referred to a standard text on sedation (Malamed, 2010) for more information.

Why is there a need for oral sedation? Simply, it is a relatively accessible means for a dentist to address patient anxiety regarding dentistry, when chairside manner is insufficient. How common is fear and anxiety? It has been estimated that over one million Canadian adults rate themselves as "very afraid" or "terrified" regarding seeing the dentist, with another two million "somewhat afraid" (Chanpong et al, 2005). Despite advances in the delivery of dentistry, this anxiety has not diminished but remained stable for 50 years (Smith and Heaton, 2003).

INDICATIONS

A basic principle in dentistry is to only use a drug if there is an indication, so this must be determined before considering giving a sedative for oral sedation. The primary indication is the presence of anxiety, fear, or phobia sufficient to prevent the delivery of needed dental care without medication. Another indication is the presence of motor dysfunction, such as that found in patients with cerebral palsy or Parkinson's disease, whose tremor or uncoordinated movements may be worsened by the anxiety of being in the dental office. Patients who are often not successfully managed by oral sedation include young children and those with cognitive impairment, such as the mentally challenged or those with dementia. These particular patients often require deep sedation or general anesthesia.

This leads to the question, what are the differences among the modalities of sedation? The official definitions are listed in Table 1 and their characteristics summarized in Table 2.

Table 1. Sedation Definitions (ADA, 2007)

Minimal sedation is a minimally depressed level of consciousness, produced by a pharmacologic method, that retains the patient's ability to maintain an airway independently and continuously and to respond normally to tactile stimulation and verbal command. Although cognitive function and coordination may be modestly impaired, ventilatory and cardiovascular functions are unaffected.
Moderate sedation is 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.
Deep sedation is a drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully after repeated or painful stimulation. The ability to maintain ventilatory function independently may be impaired. Patients may require assistance in maintaining a patent airway, and spontaneous ventilation may be inadequate. Cardiovascular function is usually maintained.
General anesthesia is a drug-induced loss of consciousness during which patients are unarousable, even by painful stimulation. The ability to maintain ventilatory function independently 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.

Table 2. Characteristics of the Levels of Sedation (RCDSO 2012a)

	MINIMAL SEDATION	MODERATE SEDATION	DEEP SEDATION	GENERAL ANESTHESIA
CONSCIOUSNESS	maintained	maintained	obtunded	unconscious
RESPONSIVENESS	to **either** verbal command **or** tactile stimulation	may require either one of or BOTH verbal command and tactile stimulation	response to repeated or painful stimuli	unarousable, even to pain
AIRWAY	maintained	no intervention required	intervention may be required	intervention usually required
PROTECTIVE REFLEXES	intact	intact	partial loss	assume absent
SPONTANEOUS VENTILATION	unaffected	adequate	may be inadequate	frequently inadequate
CARDIOVASCULAR FUNCTION	unaffected	usually maintained	usually maintained	may be impaired
REQUIRED MONITORING	basic	increased	advanced	advanced

The oral route of administration can be considered for inducing minimal or moderate sedation, but not for deeper levels. Risks are much greater in deep sedation and, as such, inducing patients to this level requires advanced training, as is found in dental anesthesia or oral and maxillofacial surgery specialty programs. It is essential to understand that a patient in moderate sedation can easily drift into deep sedation, even though that was not the intent. Thus, the practitioner must be able to recognize and manage patients who are in this latter state. As long as the patient is responding to verbal and/or tactile stimulation, then a patent airway will be maintained and protective reflexes will be intact. If the response is only to a painful stimulus, then the patient is assumed to be in a state of deep sedation, and the dentist must immediately assess and manage the airway and breathing.

Oral sedation has a number of advantages and disadvantages, as summarized in Table 3. It is easily administered and considered relatively safe, although overdoses leading to death have occurred. While swallowing pills or an elixir is not a problem for most adults, it may be for young children, those who are mentally challenged, or those with dementia. The major disadvantage of oral sedation is the inability to titrate reliably, so the dentist cannot adjust for individual patient response as can be done more easily with nitrous oxide or intravenous sedation. After a drug is taken orally, it is often risky to provide an additional dose because of variability in absorption and onset of action. There can also be a delay in drug equilibration between the plasma and the site of action, which can lead to overdose if additional doses are administered on the basis of patient anxiety (Dionne et al, 2006; Jackson et al, 2006). Thus, oral titration, or incremental dosing, is strongly discouraged. Onset of effect can vary, depending on a number of factors such as an unpredictable gastric emptying time. A further disadvantage of oral sedation is that the patient can remain under the influence of the drug postoperatively and therefore must not leave the dental office unescorted. There is very limited success in young children, as will be mentioned below. As well, the elderly are very susceptible to a more profound effect and prolonged duration of sedation, which is very problematic when considering post-operative care.

Table 3. Oral Sedation Advantages and Disadvantages

ADVANTAGES	DISADVANTAGES
Easily administered	Inability to titrate reliably
Relatively safe	Delayed and variable onset of action
Good patient acceptance	Patient must be accompanied home
	Limited success in young children
	Excessive effect and duration in the elderly

PATIENT SELECTION

To address the needs of fearful or anxious patients, the dentist must first determine its presence as part of an appropriate history. The medical history questionnaire could include a question such as "*Are you nervous during dental treatment*", as does the RCDSO's *Sample Medical History Questionnaire* (RCDSO, 2012b). The majority of these patients can be cared for with chairside manner skills inherent to dentistry. If it is determined that this will be insufficient, then modalities to induce minimal or moderate sedation, such as nitrous oxide:oxygen, oral sedation, or intravenous sedation, should be considered.

The review of the medical history will also allow a determination of the ASA Physical Status Classification. ASA I and II patients are usually suitable candidates for oral sedation. ASA III patients require more careful consideration. Techniques to control anxiety involving minimal, moderate, or possibly even deep sedation (by those trained) may be particularly valuable to ASA III patients because sedation reduces the release of endogenous catecholamines (Dionne et al, 1984). Yet, other ASA III patients could be determined to be poor candidates, emphasizing the need for thorough assessment. Patients who are ASA IV are not suitable for oral sedation, unless it is administered by those trained in deep sedation and general anesthesia. No matter what the ASA status is for the patient, his/her health should be optimized prior to the dental appointment utilizing sedation. It is prudent to have the patient followed regularly by their primary care physician.

Oral sedation for adults can be quite successful, whereas the same cannot be said for this modality in pediatrics, particularly for children under the age of 6 years (AAPD, 2006). Many young

children are not good candidates for minimal or moderate sedation techniques, and require deep sedation or general anesthesia. A recent Cochrane review of pediatric sedation (Lourenco-Matharu et al, 2012) found weak evidence that oral midazolam is effective, very weak evidence that nitrous oxide sedation is effective, and insufficient evidence to support the use of any other sedative. Doses of any agent for a child should be determined on a mg/kg basis. Minimal or moderate sedation for children should only be carried out by those with appropriate training and experience.

For the elderly, oral sedation should be used with great caution as it carries increased risks compared with younger adults. Sedatives can have more profound and prolonged action with these patients, thus side effects are more prominent and post-operative care is a concern. If this technique is to be used for the older patient, doses must be reduced significantly.

Another group of patients who require careful consideration are those who are already on CNS depressants chronically to manage a condition. In this case the dose of drug chosen for minimal or moderate sedation might have to be reduced in order to take into account the potential for additive sedative effects. Conversely, a common exception would be for those patients who chronically take drugs such as those belonging to the selective serotonin reuptake inhibitor class, such as fluoxetine (Prozac®), sertraline (Zoloft®), or paroxetine (Paxil®). If the medical history and assessment determine that these patients show no signs of sedation, then the usual doses of drug for oral sedation may be selected.

TECHNIQUE

The oral sedative should be administered to the patient in the dental office. Having the patient arrive one hour prior to the start of the appointment to take the medication is appropriate. Patients should be monitored by clinical assessment of level of consciousness, adequacy of respiration, heart rate, and blood pressure as necessary. A pulse oximeter is a very valuable monitor for oral sedation. At the end of the case, patients should be discharged to the care of a responsible adult only when they are oriented and ambulatory, have stable vital signs, and showing signs of increasing alertness. The patient should be instructed to not drive a vehicle, operate hazardous machinery, or consume alcohol for the remainder of the day.

Instructions should be given to all patients who receive oral sedation. An example for minimal sedation is shown in Table 4. As described in the RCDSO's Standard of Practice (RCDSO 2012a), a longer period to avoid solid food is required for moderate sedation.

There are two possible exceptions where it may be acceptable to have the patient take the oral sedative at home. Although rarely required, an oral sedative may be used the night before the dental appointment if the patient's anxiety regarding it would inhibit adequate sleep. A second indication for oral premedication at home, also not common, is if the patient's anxiety prevents going to the dental office. If given at home, the patient must be accompanied to the dental office by a responsible adult and must not drive to the dental office. An appropriate regimen for these two indications, assuming an ASA 1 or 2 adult, would be 0.125 to 0.25 mg of triazolam, or 5 to 10 mg of diazepam.

Table 4. Sample Patient Instructions For Minimal Sedation Using An Oral Sedative

Before your appointment
1. You must arrange to have someone drive you home at the end of your appointment and assist you to your door. You should not go home by public transit. 2. Do not wear facial makeup or nail polish. Wear comfortable, casual and loose-fitting clothing. 3. Contact us prior to the appointment if there has been a change in your general health (such as a severe cold, fever, etc.). 4. Nothing to eat or drink for 2 hours before the procedure. 5. Make a trip to the washroom just prior to being seated.
Following your appointment
1. You must **not** drive a car or operate machinery for at least 18 hours. You may be drowsy for the remainder of the day and should be recovering at home in the care of a responsible adult until you are fully alert. 2. Do not travel by public transit. 3. Do not drink any alcoholic beverages for the remainder of the day. 4. If there are any questions, do not hesitate to call our office at 123-456-7890.

An absolute wrequirement basic to the success of oral sedation is effective local anesthesia. It is not correct to assume that poor local anesthetic technique can be overcome by administering oral sedation.

It is important to note that once the sedative has been taken, it is assumed that the patient's judgment may be altered, and thus all consent issues must have been addressed pre-operatively. Any potential change in treatment plan during the appointment must have been agreed to prior to giving the sedative.

DRUGS RECOMMENDED FOR ORAL SEDATION IN DENTISTRY

Benzodiazepines are the drugs of choice for oral sedation. This is primarily due to their effectiveness and wide margin of safety. All benzodiazepines can induce the same actions in varying degrees. These actions are anxiolysis, sedation, anterograde amnesia, skeletal muscle relaxation, and anticonvulsant activity. Anxiolysis, meaning the reduction of anxiety, is the primary objective for their use in dentistry. Amnesia can be both a desired and undesired effect. Since it is anterograde, meaning it will take effect once the drug has had time for onset, patients may not recall certain aspects of the procedure. This can be beneficial if the patient were to perceive the dentistry as aversive. The drawback is that patients will not recall any postoperative instructions being given, hence these must be given in writing.

Benzodiazepines induce minimal depression of the cardiovascular and respiratory systems when given alone in therapeutic doses. Postoperative drowsiness would be expected from the sedative effect. These drugs are susceptible to abuse and patients can develop dependency. There are few contraindications, which do include myasthenia gravis, acute angle-closure glaucoma, and severe obstructive sleep apnea.

All practitioners using these drugs are required to have flumazenil, the specific benzodiazepine receptor antagonist, as one of the emergency drugs in the office. Flumazenil will cause a rapid reversal of all benzodiazepine action. This should be reserved for emergency purposes to reverse an apparent benzodiazepine overdose and only administered along with the usual emergency protocol, which includes the appropriate assessment and management of airway, breathing and circulation. Contraindications to this drug include patients taking a benzodiazepine for a seizure disorder or high doses of tricyclic antidepressants. The potential for re-sedation demands that whenever this agent is used to treat an emergency, the patient must be monitored in recovery beyond the expected duration of action of flumazenil. In practical terms, this means that the patient must be monitored for at least one hour after its administration. Flumazenil is a parenteral drug formulated as a 0.1 mg/mL injectable solution. The intended route of administration is intravenous and that is clearly best. Yet for emergency use, if venipuncture is not realistic, the practitioner should consider an intralingual/sublingual injection, while basic emergency protocol is being carried out. Using this route, an onset of action of 5 to 10 minutes may be expected.

Although all benzodiazepines share similar actions, they are differentiated by their pharmacokinetic characteristics. The agents most commonly used for oral sedation in dentistry are triazolam, diazepam, midazolam, and lorazepam. Alprazolam, temazepam and oxazepam can also be used, although there is less documentation for their use in dentistry. These are discussed next.

Triazolam is the drug of choice for oral sedation in adult dental patients. It has a rapid onset of action, short duration of effect, and a short elimination half-life, the latter reported to range from 1.5 to 5.5 hours. It has no active metabolites. These properties are ideally suited to dentistry, allowing for good onset and rapid recovery, which is important for outpatient procedures. Many years ago, reports of significant behavioral abnormalities related to triazolam were widely publicized in the lay press, but were shown to be associated with repeated use of high doses, particularly in elderly patients (Greenblatt et al, 1991; Rothschild, 1992). A significant interaction can occur with drugs that inhibit the biotransformation pathway of triazolam. Specifically, the hepatic p450 enzyme CYP3A4, which metabolizes triazolam, can be inhibited by numerous drugs, including erythromycin, clarithromycin, azole antifungals (ketoconazole, fluconazole, itraconazole), cimetidine, fluvoxamine, grapefruit juice, and several antiviral drugs including ritonavir. Concurrent administration of these agents will inhibit triazolam's breakdown, leading to increased plasma concentrations. In turn, this will lead to an increase in the degree and duration of triazolam's sedative effect. Therefore if a patient presents taking one of these agents, triazolam should not be administered, as it could result in a relative overdose.

Overall, triazolam's pharmacologic advantages make it a drug of choice for oral sedation in dentistry. In the last few years there have been periods when its availability has been reduced, necessitating that dentists seek alternatives. Otherwise, it is normally the drug to be considered first. Recommended adult doses are summarized in Table 5. It is available as 0.125 mg or 0.25 mg tablets.

Diazepam is the prototypical benzodiazepine and has a long history of use. Although it was at one time the most commonly prescribed drug, it has been superseded by other benzodiazepines, such as triazolam, that have advantageous properties. It is efficacious as an anxiolytic and sedative, but it does have several disadvantages. It has active metabolites that can cause sedation a number of hours later after the initial effect has dissipated. This is a drawback for outpatient dentistry, where short-acting agents are preferred. Recommended adult doses are summarized in Table 5. For children, doses of 0.3 to 0.6 mg/kg have been suggested (Houpt and Giovanittti, 2002). It is available as tablets (2 mg, 5 mg, and 10 mg) and as a liquid solution (1 mg/1 mL).

Lorazepam is commonly used as a sedative. It can elicit satisfactory sedation for dental procedures and has no active metabolites. It has the potential drawback in that peak effects may occur 1 to 6 hours after oral administration, making appropriate scheduling difficult. Sublingual administration using the tablets formulated for that purpose results in more predictable, and rapid, onset times. Its duration of action is expected to be longer than that found with triazolam or diazepam. Thus, it may be considered for longer dental appointments, such as over 3 hours. Recommended adult doses are summarized in Table 5. It is available as 0.5 mg, 1 mg, or 2 mg oral and sublingual tablets. Lorazepam is not recommended for pediatric patients.

Midazolam is very commonly used parenterally as part of intravenous sedation or as an adjunct in general anesthesia. Although it is not available as an oral formulation in Canada, the parenteral solution can be mixed with a sweet vehicle, such as simple syrup, and used orally. It is normally not used orally in adults, but has found use as an agent in pediatric sedation. It has a rapid onset and short duration of action. Similar to triazolam, oral midazolam is contraindicated in patients taking erythromycin or the other strong CYP3A4 inhibitors listed above because the resulting interaction can lead to increased plasma concentrations of midazolam. Midazolam's high first-pass effect leads to large differences in the parenteral and oral dosing recommendations. A dose of 0.5 mg/kg orally, up to a maximum of 15 mg, can be considered for short appointments in children. To prepare this, the 5 mg/mL parenteral solution should be diluted with an equal volume of simple syrup. A number of practitioners dilute it in acetaminophen elixir because of the sweet vehicle – this approach should only be done if the child definitely needs acetaminophen as well as the midazolam. As stated at the beginning of the article, one should never give a drug without an indication.

Alprazolam has been widely used as an anxiolytic, with less documented use for dental anxiety. Yet, it may be given for longer procedures as an alternative to lorazepam. Alprazolam is subject to the same CYP3A4 interactions as triazolam. Recommended adult doses are summarized in Table 5. It is available as 0.25 or 0.5 mg tablets for this purpose.

Temazepam is another benzodiazepine with less documented use for dental anxiety but can be considered as an alternative if triazolam is unavailable. Recommended adult doses are summarized in Table 5. It is available as 15 and 30 mg capsules.

Oxazepam, like temazepam, is another benzodiazepine with less documented use for dental anxiety but can be considered as an alternative if triazolam is unavailable. Recommended adult doses are summarized in Table 5. It is available as 10, 15 and 30 mg tablets.

Antihistamines may be considered if benzodiazepines are ruled out. All antihistamines that cross the blood:brain barrier cause sedation. These agents also have anti-cholinergic and anti-emetic effects. The former property can be useful in dentistry if hyper-salivation is a concern. The latter property can be useful if nausea is a concern. These drugs should be avoided in the elderly. Although promethazine did have wide use in the past, its side effect profile can be problematic, so it is recommended less frequently today. Diphenhydramine and dimenhydrinate can be considered, although hydroxyzine is the antihistamine that is normally recommended for use in oral sedation, particularly for children.

Hydroxyzine is the only antihistamine approved specifically as an antianxiety drug for dental procedures. It is available in either capsule or syrup formulation, the latter of which is appropriate for children. The expected duration of action is 4 to 6 hours. The suggested dose is 1 mg/kg. It is available as a 10, 25, and 50 mg capsule and a 2 mg/mL syrup.

OTHER DRUGS

There are a number of agents which have been used in the past for oral sedation, which are no longer recommended, as their risk/benefit balance is inferior to the benzodiazepines and antihistamines. For those trained only in minimal or moderate sedation techniques, agents such as chloral hydrate, opioids, ketamine, promethazine and barbiturates are not recommended as oral sedatives.

The drugs zolpidem and zaleplon are currently not available in Canada, even though the latter has been available for many years in the United States, and is very popular. If released here, they should be considered for oral sedation.

Conclusion

Oral sedation is a valuable modality that can benefit patients when it is determined that chairside manner alone is insufficient. Appropriate training is mandatory to ensure that potential risks are minimized and that the highest standards are maintained.

TABLE 5. Suggested Adult Dose Regimens For ASA I And II Patients

Dose regimens must be individualized for the patient, taking into account a number of factors including medical history and intended depth of sedation. The following regimens are suggestions only, for ASA I and II patients.

MINIMAL SEDATION	MODERATE SEDATION
Appointment 2 hours or less • triazolam 0.125-0.25 mg	**Appointment 2 hours or less** • triazolam 0.375-0.50 mg
Appointment longer than 2 hours • triazolam 0.25 mg or • diazepam 10-15 mg or • temazepam 15 mg or • oxazepam 10-15 mg	**Appointment longer than 2 hours** • triazolam 0.50 mg or • diazepam 20-30 mg or • temazepam 30 mg or • oxazepam 20-30 mg
Appointment longer than 3 hours • lorazepam 0.5-1.0 mg or • alprazolam 0.25 mg	**Appointment longer than 3 hours** • lorazepam 2.0-3.0 mg or • alprazolam 0.50 mg

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