

Introduction

Dental phobia can cause patient populations to avoid regular dental care throughout their lifetime. The goal of oral sedation is to relieve dental phobia and increase compliance during the treatment time. To adequately treat patients who may otherwise refuse basic dental care, and for commercial success, the practitioner should be familiar with oral sedation methods. This chapter is designed to familiarize clinicians with their sedation medication arsenal, the pharmacologic effects of these drugs, and techniques for safely providing oral sedation. The spectrum of sedation will be introduced and the most common classes of oral sedatives used in an outpatient setting will be reviewed including benzodiazepines, antihistaminergic agents, and opioids.

Spectrum of Sedation

Minimal Sedation: anxiolysis and is “a drug-induced state during which patients respond normally to verbal commands”

Moderate Sedation: “drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation”

Deep sedation/analgesia: “drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully, following repeated or painful stimulation”

General anesthesia: “drug-induced loss of consciousness during which patients are not arousable, even by painful stimulation”

Classes of Medications

Benzodiazepines

Benzodiazepine drugs bind the GABA chloride channels at the GABA_A receptor and increase the frequency of chloride channel activation in a GABA dependent manner. At appropriate doses, there is a very low likelihood of any significant respiratory depression. This makes them the agent of choice for most anxiety and phobia related issues, both in relation to dentistry. This class of medication has minimal cardiovascular effects in healthy patients. A study done in critically ill patients found that benzodiazepines, out of multiple classes of sedative drugs, provide the best amnestic profile while maintaining cardiac stability

Name	Onset	T(1/2)	Peak [Plasma]	Active Metabolites
Diazepam (Valium)	40 min	Up to 48 hours	1-1.5 hours	Yes
Alprazolam (Xanax)	60 min	6.3-26.9 hours	1-2 hours	No
Midazolam (Versed)	30 min	1-5 hours	20 min	No
Lorazepam (Ativan)	20-40 min	20 hours	2 hours	No
Triazolam (Halcion)	20-40 min	1.5 to 5.5 hours	2 hours	No

Histamine Blockers

Histamine blockers used for sedation act at the H1 receptors which are ubiquitous throughout the CNS neurons. These drugs block the physiologic partial depolarization of neurons caused by histamine. Thus reducing the likelihood of triggering an action potential of neurons. Their efficacy is well below that of the benzodiazepines. Because H1 blockers work independently of GABA channels, they can be used to potentiate the effects of a benzodiazepine without administering more of the benzodiazepine. These drugs are generally considered safe, with less potential for side effects than with benzodiazepines. Both drugs are historically popular for pediatric dental sedation. **Promethazine:** Readily absorbed effect within 20 min. Lasts between 4-6 hours. This drug is not addictive which differentiates it from the benzodiazepine class of drugs. Black box warning: it should not be used in children <2 years old due to fatal respiratory complications. **Hydroxyzine:** Onset is 15 to 30 min & peak effect at 2 hours. The drug effects begin to decline after 3-4 hours. Small side effect profile, mainly anticholinergic effects. Hydroxyzine is the drug of choice in pediatric patients when compared to promethazine

Opioid Sedation

Sedation with opioid medication is possible, however it is unlikely to be achieved safely via the oral route. Opioids produce primarily analgesia but can also have the effect of sedation, and respiratory depression. Opioid effects outside of analgesia are unpredictable when taken through the oral route, especially if there is no pre-operative pain. The mechanism of action of opioids are as agonists of the mu and kappa opioid receptors. An opioid in addition to a benzodiazepine has a synergistic effect to increase sedation, as well as to centrally blunt the pain response

References

- Committee on Quality Management and Departmental Administration (2019). *Continuum of Depth of Sedation: Definition of General Anesthesia and Levels of Sedation/Analgesia | American Society of Anesthesiologists (ASA)*. [online] Asahq.org. Matear, D., & Clarke, D. (1999). Considerations for the use of oral sedation in the institutionalized geriatric patient during dental interventions: a review of the literature. *Special Care In Dentistry*, 19(2), 56-63. doi: 10.1111/j.1754-4505.1999.tb01369.x
- Gill CJ, Michaelides PL. Dental drugs and anaphylactic reactions: report of a case. *Oral Sug.* 1980;50:30.
- Becker, D. (2012). Pharmacodynamic Considerations for Moderate and Deep Sedation. *Anesthesia Progress*, 59(1), 28-42. doi: 10.2344/0003-3006-59.1.28
- Malamed, S. (2018). *Sedation* (6th ed., pp. 100-114). St. Louis, MO: Elsevier.
- Tamargo, J., Le Heuzey, J., & Mabo, P. (2015). Narrow therapeutic index drugs: a clinical pharmacological consideration to flecainide. *European Journal Of Clinical Pharmacology*, 71(5), 549-567. doi: 10.1007/s00228-015-1832-0
- Donaldson, M., Gizzarelli, G., & Chanpong, B. (2007). Oral Sedation: A Primer on Anxiolysis for the Adult Patient. *Anesthesia Progress*, 54(3), 118-129. doi: 10.2344/0003-3006(2007)54[118:osapoa]2.0.co;2
- Darrouj, J., Karma, L., & Arora, R. (2009). Cardiovascular Manifestations of Sedatives and Analgesics in the Critical Care Unit. *American Journal Of Therapeutics*, 16(4), 339-353. doi: 10.1097/01.pap.0000249925.76324.47
- Jacobi, J., Fraser, G., Coursin, D., Riker, R., Fontaine, D., & Wittbrodt, E. et al. (2002). Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. *Critical Care Medicine*, 30(1), 119-141. doi: 10.1097/00003246-200201000-00020
- Mancuso, C., Tanzi, M., & Gabay, M. (2004). Paradoxical Reactions to Benzodiazepines: Literature Review and Treatment Options. *Pharmacotherapy*, 24(9), 1177-1185. doi: 10.1592/phco.24.13.1177.38089
- Bounds CG, Nelson VL. Benzodiazepines. [Updated 2018 Nov 13]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2018 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK470159/>
- Gudex, C. (1991). Adverse effects of Benzodiazepines. *Social Science & Medicine*, 33(5), 587-596. doi: 10.1016/0277-9536(91)90216-y
- McElhatton, P. (1994). The effects of benzodiazepine use during pregnancy and lactation. *Reproductive Toxicology*, 8(6), 461-475. doi: 10.1016/0890-6238(94)90029-9
- Valium [package insert] South San Francisco, CA: Roche Pharmaceuticals Inc; 2016.
- Xanax [package insert] New York, NY: Pfizer Pharmaceuticals Inc; 2011.
- Smith, M., Eadie, M., & Brophy, T. (1981). The pharmacokinetics of midazolam in man. *European Journal Of Clinical Pharmacology*, 19(4), 271-278. doi: 10.1007/bf00562804
- Midazolam drug monograph. *ClinicalKey*. Elsevier. [Available at] www.ClinicalKey.com [(Accessed 18 January 2019)]
- Ativan [package insert] Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; 2016.
- Halcion [package insert] New York, NY: Pfizer Pharmaceuticals Inc; 2016.
- Baroody, F., & Naclerio, R. (2000). Antiallergic effects of H1-receptor antagonists. *Allergy*, 55, 17-27. doi: 10.1034/j.1398-9995.2000.00803.x
- Reiner, P., & Kamondi, A. (1994). Mechanisms of antihistamine-induced sedation in the human brain: H1 receptor activation reduces a background leakage potassium current. *Neuroscience*, 59(3), 579-588. doi: 10.1016/0306-4522(94)90178-3
- Wright GZ, McAulay DJ. Current premedicating trends in pedodontics. *J Dent Child*. 1973;40:185-187.
- Phenergan [package insert] Philadelphia, PA: Wyeth Pharmaceuticals Inc
- Vistaril [package insert] New York, NY: Pfizer Labs; 2014