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Anesthetic Drugs: A Comprehensive Overview for Primary Care

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Abstract

The purpose of this document is to provide a unique white paper on the use of different anesthetic drugs within primary care clinics and the key clinical pearls for ensuring patient safety in this setting. This paper is designed to be a convenient guide that can be placed in work rooms for residents and medical school trainees to improve their learning and to provide reminders about drug-drug interactions. Finally, it is designed to be a potential living document - the first of its kind within the field. Unlike other white papers, this could be added to and modified based on the current literature and amended as newer drugs are discovered and made available. This document is intended to become a 'go-to-guide' for clinical anesthetic drug use that houses an in depth, yet condensed encyclopedia of the most pertinent, necessary information for primary care health professionals.

Keywords: Anesthesia Drugs; Drug-Drug Interactions; Primary Care; Dosage; Side Effects; Brand Names; Reference Document

Introduction

This paper is a unique document as it is unlike other papers whose main focus is on expanding knowledge or summarizing it, whereas the purpose of this document is to provide a white paper on the use of different anesthetic drugs and the key clinical pearls for ensuring patient safety. This paper is designed as a convenient guide that can be placed in work rooms for residents and medical school trainees in primary care clinics to improve their education. Additionally, it is designed to exist as a reference tool for primary care professionals on the move who may need to have quick reminders about pharmacological tips and interactions to be aware of. Finally, it is designed to be a potential living document - the first of its kind within the field. Unlike other white papers, this could be added to and modified based on the current literature and amended as newer drugs are discovered and available. Similar ideas have been proposed in other fields including neurology but are seldom followed through on. This 'go-to-guide' for anesthetic drugs serves as a living document where further reviewers can be added as contributors as well as provide additional edits to the document as it continues to 'live and breathe' for the most pertinent information. Similar to that of a Wikipedia page, the intention of this document is to exist for the purpose of being modified and added to over time.

The rationale behind the need for this type of paper is the increasing difficulty in finding this information in one centralized location. Often times, the newest and most pertinent clinical information is restricted behind pay walls as a way to force the purchase of a subscription to individual journals to gain access to the information. This is something that many primary care professionals may not have the resources to provide to their trainees. Additionally, this information may also be buried under small, randomized control trials or lost in the never-ending list of novel studies that show minor benefits. The hope of the authorial team is to create a singular centralized document that gets updated and edited as necessary with the potential for growth and modification based on the information as it becomes available. This first, improves patient safety; second, ease in teaching and educating on the topic of the different and numerous anesthetic drugs is increased; and third, providers feel more comfortable with utilizing a more diverse array of medications

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to treat the specific individualized needs of their patients. These improvements are designed to help move the field towards the goal of more individualized medicine with the patient's needs being met first and foremost.

Topical Anesthetics (3)

Benzocaine (benzocaine topical)

A local anesthetic that works by binding to sodium channels which decreases permeability of sodium ions, stabilizing the neuronal membrane, blocking initiation, and conduction of nerve impulses in the body [1-3, 94].

Usage: The benzocaine cream or spray numbs the skin or surfaces within the mouth and gums and is used for temporary pain relief, often caused by dentures and/or orthodontic appliances or injury. The cream should not be used on infants or any person under 2 years of age.

Dosage: The correct dosage is often considered the smallest amount needed to numb the area and/or to relieve pain.

Major interactions:

- Usage with other sodium channel blockers increases the risk of methemoglobinemia.
- Nitrite usage may increase an individual's risk of methemoglobinemia.

Side effects:

- Methemoglobinemia, common signs and symptoms of methemoglobinemia, which may occur within minutes to 2 hours after oral use, may include headaches, tiredness, confusion, tachycardia, light-headedness, shortness of breath, and pale, blue, or grey appearance of the skin, lips, and/or fingernails.
- Other common side effects include mild stinging, burning, or itching at the site of application, skin redness and/or tenderness, or dry, white flakes at the site of application.

Name Brands (9): Benzodent, Omedia, Oticaine, Americaine Otic, Otocain, Dermoplast, Orajel, Anbesol, and Cepacol Ultra

Lidocaine/Prilocaine (lidocaine/ prilocaine topical)

A combination medicine of local anesthetics that works by binding to voltage-gated sodium channels, inhibiting ionic fluxes that trigger nerve signals in the body [4-6, 95].

Usage: This topical medication is used to numb the skin and/or surfaces of the penis or vagina in preparation for surgery in those regions.

Dosage: By using the smallest amount needed for numbing, it should be used exactly as it is described on the prescription label up to 4 hours before a surgery or procedure. Dosing instructions on the prescription label will differ for children as lidocaine / prilocaine topical doses are based on weight in children.

Major interactions

- Acetaminophen and Aminosalicylic acid, other sodium channel blockers, nitrates, antiepileptic drugs, and sulfa drugs may all increase the risk of methemoglobinemia when used concurrently.
- This anesthetic is not recommended for teething infants and young children as it could be potentially hazardous or even fatal. Ingestion of the drug has resulted in severe brain injury, seizures, and heart problems in children.
- As lidocaine is rapidly and extensively metabolized by the liver, patients with liver disease or any form of hepatic dysfunction should be administered this drug cautiously and dosing should be modified for patients with compromised hepatic function.
- Lidocaine is primarily eliminated by the kidneys where two active metabolites, MEGX and GX, exhibit antiarrhythmic and convulsant properties. A serum concentration of these metabolites with lidocaine are increased and the half-life is prolonged in patients with renal impairment, and therefore lidocaine should be administered cautiously in patients with impaired or compromised renal function.
- Seizures could potentially occur as a result of an accumulation of active metabolites, and thus, lidocaine should be applied cautiously on patients with a past medical history of or a predisposition for seizures.

Side effects: Major side effects may include mild burning on application site, itching, rash, or changes in skin color on application site. Although uncommon, some signs of an allergic reaction may occur such as hives, swelling of the face, lips, tongue, or throat, or respiratory depression.

Name brands (25): AgonEaze, Anodyne LPT, DermacinRX Empricaine, DermacinRX Prikaan, DermacinRX Prizopak, Dolotranz, Elma, Leva Set, Lidopril, Lidopril XR, Livixil Pak, Nuvakaan II, Oraqix, Prikaan, Prilolid, Prilovix, Prilovix Lite, Prilovix Plus, Prilovix Lite Plus, Prilovix Ultralite, Prilovix Ultralite Plus, Prilovixil Plus, Relador Pak Plus, SkyaDerm-LP, and Venipuncture CPI

Lidocaine (lidocaine topical)

A topical anesthetic that is absorbed into the mucous membrane where it stabilizes the neuronal membrane by inhibiting the ionic fluxes, preventing the initiation and conduction of nerve impulses [7-10, 96].

Usage: Lidocaine topical is used to reduce discomfort or pain caused by skin irritations such as poison oak, poison ivy, poison sumac, insect bites, sunburns, burns, or scratches. Lidocaine topical is also known to treat rectal discomfort that is caused by hemorrhoids.

Dosage: Lidocaine topical may come in a variety of forms such as lotion, ointment, spray, gel, cream, skin patch, or liquid, so it is important to use as directed on the label and by using the smallest amount possible needed to numb the skin or to relieve pain.

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Major interactions

- Sodium Channel Blockers and Nitrates increase the risk of methemoglobinemia.
- Lidocaine topical is not recommended for use in young children or teething infants as ingestion could potentially be fatal or cause seizures, severe brain injury, or heart problems.
- At higher plasma levels, caused by local anesthetic toxicity, this drug could cause hypotension, bradycardia, or cardiovascular collapse and should be administered cautiously.
- Lidocaine topical should be administered cautiously to patients with impaired or compromised hepatic function.
- Serum concentrations of lidocaine and active metabolites in the kidneys are increased in patients with renal impairment, and thus, should be administered cautiously to any patient with impaired or compromised renal function.
- This drug should not be applied in high doses to any patient with a history of or a predisposition to seizures.

Side effects: Common side effects of lidocaine topical usage may include allergic reactions, mild irritation, and/or numbness where the medication has been applied.

Name brands (19): Anestacon, CidalEaze, Derma Numb, DermacinRX Lido V Pak, Eha Lotion, LidaMantle, Lidocaine Viscous, Lidopac, Lidopin, Lidovex, Lidozol, LMX 4, LMX 5, Lydexa, Medi-Quik Spray, Regenecare HA Spray, Xylocaine Jelly, Xylocaine Topical, and Ziondil.

Opioid Anesthetics (8)

Alfentanil (alfentanil systemic)

An intravenous anesthetic injection solution that exposes users to risk of addiction, abuse, and misuse. Mechanism of action involved binding to a G-protein coupled receptor (the mu-opioid receptor) that induces anti-nociception responses through the release of various neurotransmitters, including GABA, dopamine, acetylcholine, and noradrenaline [11-14, 97].

Usage: This drug is typically given to assist in relieving pain during surgery that is also used as a primary anesthesia for patients undergoing general surgery. As alfentanil systemic is an opioid, the drug is only to be given by or under direct supervision of a physician.

Dosage

- For anesthetic induction, the proper dosage should be 130-245mcg/kg, whereas the maintenance of anesthesia should be 0.5-1.5mcg/kg/min.
- Induction of MAC should be 3-8mcg/kg and the maintenance should be 3-5mcg/kg over 5-20 minutes or 0.25-1.0mcg/kg/min with a total dose of 3-50mcg/kg.
- The concentration of inhalation agents should be reduced by 30-50% for the initial hour.
- The total dosage is dependent on the duration of procedure.

Major interactions: Common interactants may include, but are not limited to any drugs that cause sleepiness or slow breathing such as opioids, sleeping pills, muscle relaxers, or medication for anxiety or seizures.

Side effects: Some of the most common side effects associated with alfentanil systemic include: blurred vision, confusion, chest pain or discomfort, dizziness, faintness, or lightheadedness, respiratory depression, headaches, nervousness, sweating, or unusual tiredness or weakness.

Name Brand (1): Alfenta.

Butorphanol (butorphanol systemic)

An opioid injection used to treat moderate to severe pain by acting as a mu-opioid receptor agonist, as well as a kappa-opioid receptor agonist [15-17, 98].

Usage: Butorphanol systemic is used as part of anesthetic for surgery or during early labor if childbirth is expected to be more than 4 hours away.

Dosage:

- The recommended initial dosage for injection is 1mg IV or 2mg IM with repeated doses every 3-4 hours as necessary.
- The standard preoperative dosage is 2mg IM given 60-90 minutes before surgery or 2mg IV shortly before induction and the maintenance in balanced anesthesia should be an incremental dose of 0.5-1.0mg IV and up to 0.06mg/kg (4mg/70kg), depending on previous sedative, analgesic, and hypnotic drugs administered.
- Rarely should a patient be given less than 4mg or more than 12.5mg, or roughly 0.06-0.18mg/kg.

Major interactions:

Common interactants may include, but are not limited to any drugs that cause sleepiness or slow breathing such as opioids, sleeping pills, muscle relaxers, or medication for anxiety or seizures.

Side effects Some of the most common side effects associated with alfentanil systemic include: blurred vision, confusion, chest pain or discomfort, dizziness, faintness, or lightheadedness, respiratory depression, headaches, nervousness, sweating, or unusual tiredness or weakness.

Name Brand (1): Stadol (no longer available in the US).

Fentanyl (fentanyl systemic)

An opioid pain medication used to treat acute, severe, or chronic pain through the selective binding and activation of mu-receptors that encourages the exchange of GTP and GDP that will then inhibits adenylate cyclase that leads to the mimicking of other opiates [18-21, 99].

Usage: Fentanyl is an incredibly versatile anesthetic drug that is used preoperatively, during surgery, and in immediate postoperative periods. In general, fentanyl is used for treating

acute pain, used in treating malignant cancer patients, and in patients with chronic pain conditions.

Dosage: The FDA has approved many programs to assist physicians for fentanyl preparations, called REMS programs.

- The typical preoperative dosage should be 50-100mcg/dose IM or slow IV over 30-60 minutes prior to surgery where adjunct to regional anesthesia should be 25-100mcg/dose slow IV over 1-2 minutes.
- For minor surgical procedures, a dosage of 0.5-2mcg/kg/dose IV should be used, whereas for a major surgery, the proper dosage should be 2-20mcg/kg/dose initially with maintenance 1-2mcg/kg/hr IV.
- Infusion should be discontinued 30-60 minutes prior to the end of surgery and adjunct to general anesthesia, although rare, should be 20-50mcg/kg/dose IV.
- The total doses should not exceed 10-15 mcg/kg for fast tracking and early extubation.

Major interactions: Common interactants may include, but are not limited to any drugs that cause sleepiness or slow breathing such as opioids, sleeping pills, muscle relaxers, or medication for anxiety or seizures.

Side effects: Some of the most common side effects associated with alfentanil systemic include: blurred vision, confusion, chest pain or discomfort, dizziness, faintness, or lightheadedness, respiratory depression, headaches, nervousness, sweating, or unusual tiredness or weakness.

Name Brands (6): Duragesic, Fentanyl Transdermal System, Sublimaze, Ionsys, Lazanda, and Fentora.

Nalbuphine (nalbuphine systemic)

An opioid pain medication used to treat moderate to severe pain, although the full mechanism of action of this drug is still not fully understood, it is believed that the drug binds to the kappa receptors of the CNS, which inhibits the neurotransmitters that mediate pain [22-26, 100].

Usage: Generally, nalbuphine is a widely-used anesthetic drug that is used to treat many different types of pain, including treating pain just after surgery or childbirth.

Dosage

- For a typical adult, based on a 70kg individual, the initial dose should be 10mg IV, IM, or subcutaneous every 3-6 hours as needed.
- For opioid non-tolerant patients, the maximum single dose is 20mg and the maximum daily dose in 160mg.
- For a typical adult, based on a 70kg individual, the induction dose for anesthesia should be 0.3-3mg/kg IV over 10-15 minutes. The maintenance dose should be 0.25-0.5mg/kg in single IV administrations as required.

Major interactions: Common interactants may include, but are not limited to any drugs that cause sleepiness or slow breathing such as opioids, sleeping pills, muscle relaxers, or medication for anxiety or seizures.

Side effects: Some of the most common side effects associated with nalbuphine systemic include: blurred vision, confusion, chest pain or discomfort, dizziness, faintness, or lightheadedness, respiratory depression, headaches, nervousness, sweating, or unusual tiredness or weakness.

Name Brand (1): Nubain.

Remifentanil (remifentanil systemic)

An opioid medication that is used to treat and/or prevent pain during and after surgery or other medical procedures. This drug acts as a mu-opioid receptor agonist, as well as an opioid analgesic [27-37, 101].

Usage: Remifentanil is most widely used in patients that require or have recently undergone a surgery or another medical procedure.

Dosage:

- If given through intubation, the induction of anesthesia should be 0.5-1mcg/kg/minute by continuous IV infusion.
- An initial dose of 1mcg/kg over 30-60 seconds may be administered as well. With nitrous oxide at 66%, the maintenance of anesthesia should be a continuous IV infusion at 0.4mcg/kg/min.
- During post-op, continuous IV infusion should be used at 0.1mcg/kg/min with every 5 minutes being adjusted in 0.025mcg/kg/min increments, where the maximum rate is 0.2mcg/kg/min.

Major interactions: Common interactants may include, but are not limited to any drugs that cause sleepiness or slow breathing such as opioids, sleeping pills, muscle relaxers, or medication for anxiety or seizures.

Side effects: Some of the most common side effects associated with remifentanil systemic include: blurred vision, confusion, chest pain or discomfort, dizziness, faintness, or lightheadedness, respiratory depression, headaches, nervousness, sweating, or unusual tiredness or weakness.

Name brand (1): Ultiva.

Sufentanil (sufentanil systemic)

An injection that is used to relieve pain during and after surgery or other medical procedures. This drug inhibits pain through the mechanism of action as acting as a mu-opioid receptor agonist [38-42, 102].

Usage: Sufentanil is widely used as a pain reliever for patients who require or have recently undergone surgery or another medical procedure such as childbirth.

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Dosage

- With incremental or infusion, if the duration of anesthesia is within 60-120 minutes, the dosage should be 1-2mcg/kg IV, where 75% or more of the total dosage may be administered prior to intubation. Maintenance dosages should be 10-25mcg IV.
- With incremental or infusion, if the duration of anesthesia is within 2-8 hours, the dosage should be 2-8mcg/kg IV, where 75% or more of the total dosage may be administered prior to intubation. Maintenance dosages should be 10-50 mcg IV.
- For patients with labor pain, the dosage should be 10-15 mcg with 10ml of bupivacaine at 0.125% with or without epinephrine and may be repeated up to 2 more times with no less than 1-hour intervals until delivery.

Major interactions: Common interactants may include, but are not limited to any drugs that cause sleepiness or slow breathing such as opioids, sleeping pills, muscle relaxers, or medication for anxiety or seizures.

Side effects: Some of the most common side effects associated with sufentanil systemic include: blurred vision, confusion, chest pain or discomfort, dizziness, faintness, or lightheadedness, respiratory depression, headaches, nervousness, sweating, or unusual tiredness or weakness.

Name brand (1): Sufenta.

Morphine (morphine systemic)

A short-acting or extended-release opioid medication used to treat pain by binding to specific opiate receptors; delta, mu, and kappa [103, 118-120].

Usage: Short-acting formulations of morphine are used to treat moderate to severe pain whereas extended-release morphine is used as an around-the-clock treatment for pain management.

Dosage

- Post-op pain dose is typically 5-20mg IV titrated.

Major interactions: Common interactants may include, but are not limited to any drugs that cause sleepiness or slow breathing such as opioids, sleeping pills, muscle relaxers, or medication for anxiety or seizures.

Side effects: Some of the most common side effects associated with morphine systemic include: blurred vision, confusion, chest pain or discomfort, dizziness, faintness, or lightheadedness, respiratory depression, headaches, nervousness, sweating, or unusual tiredness or weakness.

Name brands (11): Astramorph PF, AVINza, Duramorph, Infumorph, Kadian, Kadian ER, Morphabond, MS Contin, Oramorph SR, Roxanol, and Roxanol-T.

Hydromorphone (hydromorphone systemic)

An oral opioid medication that is seven times more potent than morphine used to treat moderate to severe pain. Treatment of pain is achieved through the binding of the mu-opioid receptor, stimulating the exchange of GTP to GDP, inhibiting cAMP, and hyperpolarizing voltage-gated potassium pumps that will reduce neuronal excitability. As metabolites do not accumulate systemically, this drug can be useful to treat severe pain in patients with renal dysfunction under close supervision [104, 121-127, 154].

Usage: Short-acting formulations of hydromorphone are used to treat moderate to severe pain whereas extended-release hydromorphone is used as an around-the-clock treatment for pain management.

Dosage:

- Oral solution should be used at 2.5-10ml every 3-6 hours as needed for pain.
- If using tablet form, 2-4mg should be taken orally every 4-6 hours.

Major interactions: Common interactants may include, but are not limited to any drugs that cause sleepiness or slow breathing such as opioids, sleeping pills, muscle relaxers, or medication for anxiety or seizures.

Side effects: Some of the most common side effects associated with hydromorphone systemic include: blurred vision, confusion, chest pain or discomfort, dizziness, faintness, or lightheadedness, respiratory depression, headaches, nervousness, sweating, or unusual tiredness or weakness.

Name brands (4): Dilaudid, Dilaudid-5, Exalgo, and Palladone.

Anticholinergic Anesthetics (3)

Glycopyrrolate (glycopyrrolate systemic)-antispas modic & bronchodilator

An anticholinergic that works by relaxing muscles in the airway to improve breathing. This drug competitively binds to muscarinic receptors and inhibits cholinergic transmission, producing relaxation in smooth muscles [64-77, 105].

Usage: Glycopyrrolate is an inhaled medication that is used to prevent airflow obstruction or bronchospasm in individuals with COPD such as emphysema and bronchitis.

Dosage:

- When used in an inhalation device, one capsule, twice daily, should be used.
- The capsule should go into the device, the mouthpiece should be clicked closed, and the buttons on the side should be pushed and released to pierce the capsule to release the medicine into the inhalation chamber.

Major interactions

- Potassium chloride or potassium citrate may increase the irritant effects of potassium on the stomach and upper intestine. Although rare, this could potentially result in ulcers, bleeding, or other gastrointestinal injuries.

- Topiramate and zonisamide can both cause increased body temperature with decreased sweating, which may be worsened if combined with glycopyrrolate. Heat stroke and hospitalization may occur in some people, specifically in children, and may be more likely in warm weather or during exercise.
- Cold or allergy medications that contain an antihistamine, medicine to treat Parkinson's disease, medicine to treat excess stomach acid, ulcers, motion sickness, or irritable bowel syndrome, bladder or urinary medicines, or other bronchodilators can all potentially have a negative effect when taken with glycopyrrolate.

Side effects: Side effects of glycopyrrolate may include, but are not limited to wheezing, choking, or any other breathing problems, blurred vision, eye pain, nausea, painful or difficult urination, congestion, sneezing, sore throat, or vomiting.

Name brand (1): Glyrx-PF – antispasmodic.

Atropine (atropine systemic) -antispasmodic & bronchodilator

A drug given during anesthesia to help keep the heartbeat normal during surgery. This drug works by acting as a sympathetic, competitive antagonist of the muscarinic cholinergic receptors, reducing the effects of the parasympathetic stimulation [86-93, 106].

Usage: Atropine is used to treat the symptoms of bradycardia as well as to decrease salivation and bronchial secretions before and during surgery. It is also used as an antidote for overdose of cholinergic drugs or mushroom poisoning.

Dosage:

- Atropine can be administered by IV, subcutaneous, intramuscular, or endotracheal (ET), although IV is preferred.
- The correct dosage of atropine in a typical adult should be 0.4-1.0mg every 1-2 hours as needed.
- When ET administration is used in an adult patient, dilute 1-2mg in 10ml of sterile water or normal saline beforehand. For pediatric patients, double the usual IV dosage and dilute in 3-5ml.
- When treating antisialagogue/anti-vagal, 0.5-1.0mg every 1-2 hours.
- When treating organophosphate or muscarinic poisoning, 2-3mg every 20-30 minutes; doses up to 20mg titrated to effect for secretion control may be required.
- When treating bradycardia, 1-3mg every 3-5 minutes and repeated until obtaining the desired heart rate. This will be most effective for sinus and AV nodal disease.
- For pediatric patients, the proper dosage should be 0.01-0.03mg/kg every 3-5 minutes, where the minimum dose is 0.1mg. In a child, the maximum dose is 0.5mg and in an adolescent, the maximum dose is 1.0mg. The maximum cumulative dose is 1.0mg in a child and 2.0mg in an adolescent.
- For rapid sequence intubation pretreatment, the proper dosage is 0.01mg/kg IV for adults with bradycardia secondary to repeat dosing of succinylcholine. Pediatric dosage should be 0.02mg/kg IV, where the minimum dosage should be 0.1mg. This is not recommended as a routine treatment option.

Major interactions:

- Potassium chloride or potassium citrate may increase the irritant effects of potassium on the stomach and upper intestine. Although rare, this could potentially result in ulcers, bleeding, or other gastrointestinal injuries.
- Topiramate and zonisamide can both cause increased body temperature with decreased sweating, which may be worsened if combined with glycopyrrolate. Heat stroke and hospitalization may occur in some people, specifically in children, and may be more likely in warm weather or during exercise.

Side effects: Atropine may potentially cause various side effects that include, but are not limited to hypersensitivity reactions, sinus tachycardia, blepharitis, decreased visual acuity, decreased food absorption, lethargy, chest pain, insomnia, dehydration, paranoia, anxiety, atrial fibrillation, headaches, dizziness, blurred vision, vertigo, nausea, or vomiting.

Name brands (3): AtroPen, Atreza, and Sal-Tropine.

Hyoscyamine (hyoscyamine systemic) – antispasmodic

An antispasmodic medication that comes in many forms such as oral liquid, solution, and tablet to treat many different medical conditions. This drug is a non-selective competitive antagonist of the muscarinic receptors that leads to the inhibition of the parasympathetic activities of acetylcholine [78-85, 107].

Usage: Hyoscyamine is used to treat many different intestinal and stomach disorders such as peptic ulcers, irritable bowel syndrome as well as to control muscle spasms in the digestive tract, kidneys, and bladder. Hyoscyamine is also used to reduce stomach acid, reduce tremors and rigid muscles, and as a drying agent to control excessive salivation, runny nose, or excessive sweating.

Dosage:

- Pre-anesthetic dose should be 0.005mg/kg IM, IV, or subcutaneous injection 30-60 minutes prior to anticipated start time of anesthesia or at the same time preanesthetic narcotic/sedatives are given.
- During surgery, a dose of 0.125mg IV once and repeated in increments of 0.125mg as needed to reduce drug-induced bradycardia.
- Extended-release tablets should be swallowed whole, never crushed, chewed, or broken.
- When in liquid form, it should be measured carefully, using the dosing syringe provided or a medicine dose measuring device.

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Major interactions

- Potassium chloride or potassium citrate may increase the irritant effects of potassium on the stomach and upper intestine and could potentially result in ulcers, bleeding, or other gastrointestinal injuries.
- Topiramate and zonisamide can both cause increased body temperature with decreased sweating, which may be worsened if combined with hyoscyamine. Heat stroke and hospitalization may occur in some people, specifically in children, and may be more likely in warm weather or during exercise.
- Other medications that may potentially interact with hyoscyamine include, but are not limited to antidepressants or any medicine to treat mental illnesses, cold or allergy medication, antinausea medications, or an MAO inhibitor.

Side effects: Hyoscyamine may potentially cause various side effects that include, but are not limited to anxiety, hallucinations, confusion, slurred speech, memory problems, diarrhea, dizziness, rash, dry mouth, decreased sense of taste, nausea, bloating, constipation, headache, insomnia, impotence, vomiting, or blurred vision.

Name brands (15): Anazpaz, Colidrops, Ed-Spaz, HyoMax, HyoMax DT, HyoMax FT, HyoMax SL, HyoMax SR, Hyosyne, Levbid, Levsin, Levsin SL, Oscimin, Symax Duotab, Symax SL, and Symax SR.

Local Injectable Anesthetics (6)

Articaine/Epinephrine (articaine/ epinephrine systemic)

A combination anesthetic that works by blocking nerve signals in the body through the binding to sodium channels that will reduce sodium influx and threshold cannot be met for neuronal firing [56-63, 108].

Usage: Articaine/epinephrine is most commonly used as a numbing agent for the mouth during dental procedures by injection into the gum area.

Dosage

- For infiltration, 0.5-2.5ml or 20-100mg of articaine.
- For nerve blocking, 0.5-3.4ml or 20-136mg of articaine.
- For oral surgery, 1.0-5.1ml or 40-204mg of articaine.
- For most routine dental procedures, the preferred articaine-epinephrine ratio should be 1:200,000.

Major interactions: More common interactants may include, but are not limited to antidepressants, antipsychotic medications, or an MAO inhibitor. Medication such as an articaine/epinephrine combination could potentially interact with many other drugs and cause dangerous side effects, or even death. A total list consisting of 38 major interactions and 191 moderate interactions should be reviewed fully before prescribing.

Side effects: Common side effects of the articaine/epinephrine combination anesthetic include, but are not limited to tongue pain or swelling, headache, mild swelling in the face, shallow breathing, blurred vision, anxiety, bradycardia, confusion, numbness, or a tingling sensation.

Name brands (6): Articadent, Orabloc, Septocaine, Ultacan, Ultacan Forte, and Zorcaine.

Lidocaine (lidocaine systemic) – group 1 antiarrhythmics

An anesthetic that causes numbness to the specific area of the body where injected to reduce pain or discomfort by stabilizing the neuronal membrane by binding to and inhibiting voltage-gated sodium channels [7-10, 109].

Usage: Injectable forms of lidocaine are often used as a numbing agent to aid in reducing pain or discomfort caused by invasive medical procedures. Additionally, this form of lidocaine is used to treat irregular heart rhythms that may signal a possible heart attack as well as acting as an epidural to reduce the discomforts of contractions during labor.

Dosage:

- For adult patients in ventricular fibrillation, ventricular tachycardia, or cardiac arrhythmia, the initial dose should be 50-100mg IV over 2-3 minutes and may be repeated after 5 minutes, if necessary, where 300mg in a 1-hour period is not exceeded.
- For adult patients needing anesthesia, the maximum individual dose should be 4mg/kg IV with 4.5mg/kg for infiltration, where the maximum total dose is 300mg.

Major interactions: More common interactants may include, but are not limited to nefazodone, antibiotics, St John's wort, antiviral medicine to treat hepatitis or HIV/AIDS, seizure medications, tuberculosis medications, or heart or blood pressure medications. Medication such as lidocaine could potentially interact with many other drugs and cause dangerous side effects, or even death. A total list consisting of 14 major interactions and 149 moderate interactions should be reviewed fully before prescribing.

Side effects: Some common side effects of lidocaine may include, but are not limited to shallow breathing, feeling faint, muscle stiffness, bradycardia, nausea, dizziness, anxiety, confusion, blue appearance of the skin, or vomiting.

Name brands (3): DentiPatch, Xylocaine HCI, and Xylocaine-MPF.

Tetracaine (tetracaine systemic)

A local anesthetic that works by reversibly binds voltage-gated sodium ion channels in neuronal cell membranes, preventing the initiation and conduction of nerve impulses [51-55, 110].

Usage: Tetracaine is most often given as an epidural injection to produce numbness during labor, surgery, or other medical procedures.

Dosage:

- For adult patients, the maximum single dose should be 1-3mg/kg without a vasoconstrictor or 1.5mg/kg with a vasoconstrictor.

Major interactions:

- Bupivacaine liposome could potentially alter the release rate if exposed to another local anesthetic solution such as tetracaine. If injected into the same area around the same time, bupivacaine liposome could potentially cause a rapid release of the active medication and alter the safety and efficiency of each other. Additional use of local anesthetics should be generally avoided within 96 hours following administration of bupivacaine liposome.
- Sodium nitrite usage may increase an individual's risk of methemoglobinemia.
- Other medicines such as sulfa drugs may potentially cause adverse effects when used alongside tetracaine.

Side effects: Some potential side effects of tetracaine may include, but are not limited to lightheadedness, headaches, shallow breathing, dizziness, chills, tingling sensations, blurred vision, tremors, nausea, ringing in the ears, or vomiting.

Name brands (3): Pontocaine, Democaine, and Viractin.

Ropivacaine (ropivacaine systemic)

An injectable anesthetic solution that binds to voltage-gated sodium ion channels in the neuronal membrane [111, 128-132].

Usage: Ropivacaine is used as a local anesthetic for a spinal block, or an epidural, to provide anesthesia during a surgery or C-section, or to ease labor pains.

Dosage:

- For lumbar epidural administration for surgery, the typical adult dose for a 0.5% concentrated solution should be 75-150mg, which should have a duration of 2-4 hours. For a 0.75% concentration, 113-188mg, which should have a duration of 3-5 hours. For a 1.0% concentration, 150-200mg, which should have a duration for 4-6 hours.
- If administering for a C-section in a typical adult, a 0.5% concentrated solution should be 100-150mg, which should have a duration of 2-4 hours. With a 0.75% concentration, 113-150mg, which should have a duration of 3-5 hours.
- When administered for a typical adult with labor pain, the initial dose should be 20-40mg of a 0.2% concentrated solution, which should last 0.5-1.5 hours, with a continuous infusion of 12-28mg/hr.

Major interactions:

- Bupivacaine liposome could potentially alter the release rate if exposed to another sodium channel block. If injected into the same area around the same time, bupivacaine liposome could potentially cause a rapid release of the active medication and alter the safety and efficiency of each other. Additional use of local anesthetics should be generally avoided within 96 hours following administration of bupivacaine liposome.
- Sodium Channel blocker usage may increase an individual's risk of methemoglobinemia.

Side effects: Potentially dangerous side effects may include, but are not limited to anxiousness, confusion, issues with speech or vision, ringing in the ears, metallic taste, seizures, bradycardia or tachycardia, problems with urination or sexual function, back pain, nausea, or vomiting.

Name brands (4): Naropin, Naropin Polyamp, Naropin SDV, and Naropin Novaplus.

Bupivacaine (bupivacaine systemic)

An injectable local anesthetic solution with many practical medical uses due to its ability to reversibly bind to specific sodium ion channels in the neuronal membrane, reducing the permeability of sodium ions and resulting in the loss of sensation [112, 133-135].

Usage: Bupivacaine is given as an epidural injection into the spinal column to produce numbness during labor, surgery, or other certain medical or dental procedures.

Dosage:

- In a typical adult patient for an epidural block, 75-150mg of a 0.75% concentrated solution should be given for a complete motor block; 50-100mg of a 0.5% solution for a moderate to complete motor block; and 25-50mg of a 0.25% solution for partial to moderate motor block.
- For epidural anesthesia, 0.5% and 0.75% solutions should be administered in 3-5ml increments.
- For epidural anesthesia in obstetrics, only 0.5% and 0.25% concentrations should be used, where the 0.5% solution should be administered in 3-5ml increments and not exceeding 50-100mg at any dosing interval.

Major interactions

- Bupivacaine liposome could potentially alter the release rate if exposed to another local anesthetic solution such as ropivacaine. If injected into the same area around the same time, bupivacaine liposome could potentially cause a rapid release of the active medication and alter the safety and efficiency of each other. Additional use of local anesthetics should be generally avoided within 96 hours following administration of bupivacaine liposome.
- Prilocaine usage may increase an individual's risk of methemoglobinemia.

Side effects: Potentially dangerous side effects may include, but are not limited to anxiousness, confusion, issues with speech or vision, ringing in the ears, metallic taste, seizures, bradycardia or tachycardia, problems with urination or sexual function, back pain, nausea, or vomiting.

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Name Brands (5): Marcaine HCl, Marcaine Spinal, Sensorcaine, Sensorcaine-MPF, and Sensorcaine-MPF Spinal

Chloroprocaine (chloroprocaine systemic)

A fast-onset injectable local anesthetic solution to produce local anesthesia by infiltration and peripheral nerve block. This drug acts by increasing the threshold required for electrical excitation of nerves [113, 136-139].

Usage: Chloroprocaine is used most commonly to establish adequate epidural anesthesia as well as for peripheral nerve block in a patient undergoing short ambulatory surgery that is not anticipated to produce significant postoperative pain.

Dosage:

- For lumbar epidural anesthesia for C-section delivery in a typical adult patient should be a total dose of 15-25ml of a 3.0% preservative-free solution.
- For infiltration and peripheral nerve block:
- Digital without epinephrine should be 3-4ml of a 1.0% solution with a total dose of 30-40mg.
- Infraorbital should be 0.5-1.0ml of a 2.0% solution with a total dose of 10-20mg.
- Mandibular should be 2-3ml of a 2.0% solution for a total dose of 40-60mg.
- Paracervical should be 3ml per each of four sites of a 1.0% solution with a total dose of up to 120mg.
- Pudendal should be 10ml for each side of a 2.0% solution with a total dose of 400mg.

Major interactions

- Bupivacaine liposome could potentially alter the release rate if exposed to another sodium channel blockers. If injected into the same area around the same time, bupivacaine liposome could potentially cause a rapid release of the active medication and alter the safety and efficiency of each other. Additional use of local anesthetics should be generally avoided within 96 hours following administration of bupivacaine liposome.
- Nitrite usage may increase an individual's risk of methemoglo binemia.

Side effects: Dangerous side effects of chloroprocaine may include, but are not limited to hyperhidrosis, severe anxiety, lightheadedness, confusion, headaches, change in speech, tremors, dizziness, blurred vision, seizures, bradycardia or tachycardia, chest pain, leaking of urine or stool, back pain, or sexual dysfunction.

Name brands (2): Nesacaine and Nesacaine-MPF.

Benzodiazepine Anesthetics (4)

Remimazolam (remimazolam systemic)

An injectable anesthetic and sedative that binds to brain benzodiazepine receptors with high affinity, which facilitates the opening of GABA activated chloride channels and leads to the decrease in neuron firing and produces an inhibitory response [43-50, 114].

Usage: Remimazolam is most often used as a means for maintaining relaxation or sleep in patients undergoing medical procedures that last 30 minutes or less.

Dosage:

- For adult patients, the induction dose should be 5mg IV over one minute, while maintenance dosages should be 2.5mg IV over 15 seconds.

Major interactions: Medication such as remimazolam could potentially interact with many other drugs and cause dangerous side effects, or even death. A total list consisting of 31 major interactions and 272 moderate interactions should be reviewed fully before prescribing.

Side effects: Remimazolam has many potential side effects which include, but are not limited to blurred vision, dizziness, irregular heartbeat, nausea, sweating, body aches, chills, fever, congestion, sore throat, insomnia, disorientation, pale or blue lips, fingernails, or skin, mood changes, shakiness, or vomiting.

Name brand (1): Byfavo.

Diazepam (diazepam systemic)

An oral anesthetic medication that works by enhancing the activity of certain neurotransmitters in the brain through the binding of GABA receptors found in the limbic system and hypothalamus [115, 140-144].

Usage: Diazepam is used to treat anxiety disorders, alcohol withdrawal symptoms, or muscle spasms. Diazepam is sometimes also used with other medications to treat seizures.

Dosage:

- For light anesthesia in a typical adult, the correct preoperative dose should be 10mg IM once before surgery.
- For muscle spasms in a typical adult, a dose of 2-10mg, 3-4 times per day should be taken orally.

Major interactions: Medication such as diazepam could potentially interact with many other drugs and cause dangerous side effects, or even death. A total list consisting of 30 major interactions and 379 moderate interactions should be reviewed fully before prescribing. More common interactants may include, but are not limited to any drugs that cause sleepiness or slow breathing such as opioids, sleeping pills, muscle relaxers, or medication for depression or seizures.

Side effects: Diazepam has many potential side effects which include, but are not limited to blurred vision, dizziness, irregular heartbeat, nausea, sweating, body aches, chills, fever, congestion, sore throat, insomnia, disorientation, pale or blue lips, fingernails, or skin, mood changes, shakiness, or vomiting.

Name brands (4): Diastat, Diastat AcuDial, Valium, and Valtoco.

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Table 1: Summary.

Drug Name	Adult Dosing	Major Interactants	Major Side Effects
Alfentanil Systemic	Induction, 130-245mcg/kg. Maintenance, 0.5-1.5mcg/kg/min.	Any drugs that cause sleepiness or slow breathing	Respiratory depression Blurred vision Chest pain
Articaine / Epinephrine Systemic	Infiltration, 20-100mg. Nerve blocking, 20-136mg. Oral surgery, 40-204mg.	Antidepressants Antipsychotics MAO inhibitor	Tongue pain Swelling of the face Bradycardia
Atropine Systemic	0.4-1.0mg every 1-2 hours as needed.	Potassium chloride or potassium citrate Topiramate and zonisamide	Atrial fibrillation Decreased food absorption Decreased visual acuity Blepharitis Sinus tachycardia
Benzocaine Topical	The smallest amount needed to numb the area and/or to relieve pain.	Other sodium channel blockers Nitrite	Methemoglobinemia Mild stinging, burning, or itching at the site of application
Bupivacaine Systemic	75-150mg of a 0.75% concentrated solution for a complete motor block; 50-100mg of a 0.5% solution for a moderate to complete motor block; and 25-50mg of a 0.25% solution for partial to moderate motor block.	Bupivacaine liposome Prilocaine	Seizures Ringing in the ears Metallic taste Urination problems Sexual dysfunction Nausea/vomiting Back pain
Butorphanol Systemic	1mg IV or 2mg IM with repeated doses every 3-4 hours as necessary.	Any drugs that cause sleepiness or slow breathing	Respiratory depression Blurred vision Chest pain
Chloroprocaine Systemic	Total dose, 15-25ml of a 3.0% preservative-free solution.	Bupivacaine liposome Nitrites	Seizures Tremors Hyperhidrosis
Diazepam Systemic	10mg IM once before surgery.	Total list of 30 major interactants should be reviewed Any drugs that cause sleepiness or slow breathing	Insomnia Nausea/vomiting Pale/blue lips, skin, or fingernails Irregular heartbeat Shakiness Mood changes Disorientation
Fentanyl Systemic	Minor surgeries, 0.5-2mcg/kg/dose IV should be used. Major surgeries, 2-20mcg/kg/dose. Maintenance is 1-2mcg/kg/hr IV.	Any drugs that cause sleepiness or slow breathing	Respiratory depression Blurred vision Chest pain Unusual tiredness or weakness
Glycopyrrolate Systemic	In an inhalation device, one capsule, twice daily.	Potassium chloride or potassium citrate Topiramate and zonisamide Cold or allergy medications that contain an antihistamine	Choking Breathing problems Eye pain Nausea/vomiting Painful urination Blurred vision Sneezing
Hydromorphone Systemic	Oral solution, 2.5-10ml every 3-6 hours as needed.	Any drugs that cause sleepiness or slow breathing	Respiratory depression Blurred vision Chest pain
Hyoscyamine Systemic	30-60min before surgery, 0.005mg/kg IM, IV, or subcutaneous injection. During surgery, 0.125mg IV once and repeated in identical increments as needed.	Potassium chloride or potassium citrate Topiramate and zonisamide Antidepressants Cold or allergy medication	Insomnia Impotence Nausea/vomiting Decreased taste Constipation Diarrhea Slurred speech
Lidocaine Systemic	Induction, 50-100mg IV over 2-3 minutes and may be repeated after 5 mins.	Nefazodone Antibiotics Antivirals for hepatitis or HIV/AIDS St John's wort Seizure medications Tuberculosis medications Heart/blood pressure medications	Shallow breathing Bradycardia Nausea/vomiting Blue appearance of the skin Anxiety Muscle stiffness Confusion Dizziness Feeling faint

Lidocaine Topical	The smallest amount possible needed to numb the skin or to relieve pain.	Sodium channel blockers Nitrates	Mild stinging, burning, or itching at the site of application
Lidocaine / Prilocaine Topical	The smallest amount possible needed to numb the skin or to relieve pain.	Acetaminophen Aminosalicylic acid Other sodium channel blockers Nitrates Antiepileptic drugs Sulfa drugs	Mild stinging, burning, or itching at the site of application
Lorazepam Systemic	IM, 0.05mg/kg with a max of 4mg; OR 2mg IV total or 0.044mg/kg (whichever is smaller).	Total list of 29 major interactants should be reviewed Any drugs that cause sleepiness or slow breathing	Jaundice Dark urine Mood changes Feeling unsteady Changes in vision Drowsiness Confusion
Midazolam Systemic	0.01-0.05mg/kg IV over several minutes and repeated every 10–15-mins. Maintenance, 0.1-0.2mg/kg IV per hour.	Total list of 34 major interactants should be reviewed Any drugs that cause sleepiness or slow breathing	Insomnia Nausea/vomiting Pale/blue lips, skin, or fingernails Irregular heartbeat Shakiness Mood changes Disorientation
Morphine Systemic	Post-op, 5-20mg IV titrated.	Any drugs that cause sleepiness or slow breathing	Respiratory depression Blurred vision Chest pain
Nalbuphine Systemic	Induction, 0.3-3mg/kg IV over 10-15 mins. Maintenance, 0.25-0.5mg/kg in single IV administrations as required.	Any drugs that cause sleepiness or slow breathing	Respiratory depression Blurred vision Chest pain
Remifentanil Systemic	Induction, 0.5-1mcg/kg/minute by continuous IV. With nitrous oxide at 66%, maintenance should be continuous IV at 0.4mcg/kg/min.	Any drugs that cause sleepiness or slow breathing	Respiratory depression Blurred vision Chest pain Unusual tiredness or weakness
Remimazolam Systemic	Induction, 5mg IV over 1 min. Maintenance, 2.5mg IV over 15 seconds.	Total list of 31 major interactants should be reviewed	Insomnia Nausea/vomiting Pale/blue lips, skin, or fingernails
Ropivacaine Systemic	0.5% concentrated solution, 75-150mg. 0.75% solution, 113-188mg. 1.0% solution, 150-200mg.	Bupivacaine liposome Sodium channel blockers	Urination problems Sexual dysfunction Ringing in the ears Nausea/vomiting Back pain Seizures Metallic taste
Sufentanil Systemic	For 60-120 mins, 1-2mcg/kg IV. Maintenance, 10-25mcg IV. For 2-8 hours, 2-8mcg/kg IV. Maintenance, 10-50 mcg IV.	Any drugs that cause sleepiness or slow breathing	Respiratory depression Blurred vision Chest pain Unusual tiredness or weakness
Tetracaine Systemic	Max single dose, 1-3mg/kg w/o a vasoconstrictor; 1.5mg/kg with a vasoconstrictor.	Bupivacaine liposome Sodium nitrite Sulfa drugs	Ringing in the ears Tremors Nausea/vomiting Shallow breathing

Midazolam (midazolam systemic)

An oral anesthetic medication used for sedation that is five times more potent than diazepam. This drug achieves these characteristics by binding to the GABA receptor-chloride ionophore complex in the CNS, opening chloride channels, and increases the inhibitory effect of GABA on the CNS [116, 145-149].

Usage: Midazolam is used to sedate patients who are having minor surgeries, dental work, or other specific medical procedures.

Dosage:

- For light sedation in a typical adult under 60 years, 0.07-0.08mg/kg IM should be administered up to 1 hour before surgery. If given by IV, 1.0-2.5mg every 2 minutes should be used with a maintenance dose of 25% increments of the initial dose to reach sedation with a maximum dose of 2.5mg/dose.
- For light anesthesia in a premedicated typical adult patient, 0.25mg/kg IV should be administered over 20-30 seconds. For non-premedicated patients, an initial dose of 0.3-0.35mg/kg IV should be used over 20-30 seconds with a maximum dose of 0.6mg/kg.
- For sedation in a typical adult patient, the initial dose should be 0.01-0.05mg/kg IV via slow injection over several minutes and may be repeated in 10–15-minute intervals until sedation is achieved with a maintenance dose of 0.1-0.2mg/kg IV per hour.

Major interactions: Medication such as midazolam could potentially interact with many other drugs and cause dangerous side effects, or even death. A total list consisting of 34 major interactions and 391 moderate interactions should be reviewed fully before prescribing. More common interactants may include, but are not limited to any drugs that cause sleepiness or slow breathing such as opioids, sleeping pills, muscle relaxers, or medication for anxiety or seizures.

Side effects: Some side effects of midazolam may include, but are not limited to blurred vision, dizziness, irregular heartbeat, nausea, sweating, body aches, chills, fever, congestion, sore throat, insomnia, disorientation, pale or blue lips, fingernails, or skin, mood changes, shakiness, or vomiting.

Name brands (3): Nayzilam, Seizalam, and Versed.

Lorazepam (lorazepam systemic)

An oral anesthetic medication designed to produce a calming effect that is five times more potent than midazolam. This drug enhances the effect of the inhibitory neurotransmitter gamma-aminobutyric acid on the GABA receptors by binding to a site that is distinct from the GABA binding site in the CNS [117, 150-153].

Usage: Lorazepam is most commonly used to treat anxiety in patients to help them relax before an operation or other medical or dental treatment.

Dosage:

- For anxiety in the typical adult patient, the initial dose should be 2-3mg orally per day and can be given 2-3 times per day with a maintenance dose of 1-2mg orally, 2-3 times per day.
- For light anesthesia in a typical adult patient, an IM injection of 0.05mg/kg should be given once with a maximum dose of 4mg. If given by IV, 2mg total or 0.044mg/kg should be given once (whichever is a smaller dose).

Major interactions: Medication such as lorazepam could potentially interact with many other drugs and cause dangerous side effects, or even death. A total list consisting of 29 major interactions and 296 moderate interactions should be reviewed fully before prescribing. More common interactants may include, but are not limited to any drugs that cause sleepiness or slow breathing such as opioids, sleeping pills, muscle relaxers, or medication for depression or seizures.

Side effects: Potential side effects of lorazepam may include, but are not limited to severe drowsiness, unusual changes in mood or behavior, confusion, insomnia, changes in vision, dark urine, drowsiness, feeling unsteady, dizziness, or jaundice.

Name brands (2): Ativan and Lorazepam Intensol.

Conclusion

The purpose of this paper is to provide a clear and easy means to navigate a document on the use of different anesthetic drugs and the key clinical pearls for ensuring patient safety. Through gathering this key information into a singular document, this paper can be utilized as a convenient guide in work rooms for residents and medical school trainees. This paper is designed around the idea that the practice of medicine and the understanding of how to utilize the currently available medications should be easy to access, therefore, it is simply a summary of what is known at the time of writing. With this in mind, the paper was designed to be a potential living document - which could be added to and modified based on the current literature and amended as newer drugs are discovered and available. This would allow for further reviewers and/or authors to be added as contributors in the future as more is learned about the utilization of these drugs.

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