Becoming an Anesthetic Mixologist

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There are literally thousands of combinations of sedatives/tranquilizers, muscle relaxers, neurosteriods, opioids, dissociative agents, paralytics and so on to choose from. Selecting what is safe, practical and even cost efficient is necessary for our patients, keeping in mind the specific signlamnet and health status of our individual patient.

Benzodiazepines are reported to enhance the positive subjective effects of opioids (euphoria) but it is unclear whether the reinforcing effects are additive or synergistic. Either way we see a great MAC sparing effect with the combination of the two medications.

When creating a multimodal anesthetic plan utilizing volatile anesthetic or TIVA we should always consider this formula.

Analgesia + Muscle relaxation + Sedation

Often one of these medication on the equation will have anxiolytic effects as well.

OPIOID CONTINUOUS RATE INFUSIONS
Premedication with a mu opioid agonist will provide an effective loading dose for any mu opioid CRI

Fentanyl (50mcg/mL or 0.05mg/mL)

- Commonly used in a CRI as the sole agent or can be combined with ketamine +/- lidocaine.
- A single IV bolus will only last approximately 20-30 minutes.
- Fentanyl has a context sensitive half life. When used as a CRI for greater than 2 hours the drug will start to accumulate in the tissues. Once accumulation has occurred the plasma concentration does not decrease rapidly once the CRI is discontinued. To prevent a prolonged recovery, it may be beneficial to decrease the fentanyl CRI rate and/or make adjustments to the vaporizer about 30-40 minutes prior to the end of surgery. The effects tend to last much longer in cats compared to dogs.
- Extremely high dosages may depress ventilation and cause bradycardia.
- Fentanyl does not require dilution when used in a syringe pump
- An IV bolus (loading dosage) of 1-5mcg/kg should be given prior to the start of the CRI if no other mu agonist opioid has been administered.
- CRI rate (intra-op): 0.1-0.7mcg/kg/min (6-42mcg/kg/hr) **It is recommended to start with 0.1mcg/kg/min and adjust the dosage up as needed depending on patient response to surgical stimulus. If the patient responds to surgical stimulation then it is recommended that a bolus (1-3mcg/kg) be administered and the CRI rate increased in 0.1 increments until no further surgical stimulation occurs.
- CRI rate (post-op): 0.03-0.05mcg/kg/min (2-3mcg/kg/hr)

Remifentanil (1mg powder)

- Commonly used alone in a CRI or can be combined with ketamine +/- lidocaine.
- Metabolized by nonspecific plasma esterases to inactive metabolites. This makes remifentanil superior to fentanyl for patients with renal or hepatic dysfunction.
- Rapid onset of action and short duration of action. It must be administered as a CRI because the short duration of action limits the use as a bolus injection.
- It has non-cumulative effects within the body so recovery is rapid after CRI is discontinued.
- Extremely high dosages may cause profound sedation, respiratory depression and bradycardia.
- Supplied as a 1mg powder that must be reconstituted with sterile saline prior to use.

Dilution: mix 1mg powder in 20mL NaCl → 50mcg/mL or mix 1mg powder in 10mL NaCl → 100mcg/mL
- Loading dosage: 1-5mcg/kg IV should be given prior to the start of the CRI if no other mu agonist opioid has been administered.
- CRI rate: 0.1-0.7 mcg/kg/min

Hydromorphone (2mg/mL)
- Can be used alone or in combination with ketamine +/- lidocaine.
- Does not cause histamine release.
- Dilution: add 2mg (1mL) to 9mL NaCl → 0.2mg/mL
- Loading dosage: 0.03-0.05mg/kg IV prior to starting the CRI if no other mu agonist opioid has been administered.
- CRI rate: 0.3-0.8mcg/kg/min (0.02-0.05mg/kg/hr)

Morphine (15mg/mL)
- Commonly used alone or in combination with ketamine +/- lidocaine.
- Caution with use in cats. Morphine CRIs are not commonly administered alone to cats when awake due to the likelihood of causing excitation.
- Morphine is light sensitive. The syringe or fluid bag should be covered when using a morphine CRI long term.
- Dilution: add 15mg (1mL) to 9mL NaCl → 1.5mg/mL or add 30mg (2mL) to 8mL NaCl → 3mg/mL
- Loading dosage: 0.1-0.2mg/kg IV (very slowly) should be given prior to the start of the CRI if no other mu agonist opioid has been administered.
- CRI rate: 2-6mcg/kg/min (0.1-0.3mg/kg/hr)

Methadone (10mg/mL)
- Can be used alone or in combination with ketamine +/- lidocaine.
- Also acts as an NMDA receptor antagonist to help treat and prevent central sensitization.
- Dilution: add 10mg (1mL) to 9mL NaCl → 1mg/mL
- Loading dosage: 0.1-0.5mg/kg IV prior to starting the CRI if no other mu agonist opioid has been administered.
- CRI rate: 0.05-2mg/kg/hr

ADJUNCT CRIs FOR ADDITIONAL PAIN MANAGEMENT

Ketamine (100mg/mL)
- Classified as an NMDA receptor antagonist that effectively blocks central sensitization from occurring in the dorsal horn of the spinal cord and helps prevent hyperalgesia and allodynia.
- Ketamine does not have any direct analgesic effects but it is used as an adjunct to other analgesic drugs such as opioids. It may help improve opioid receptor sensitivity. DO NOT use ketamine as the sole analgesic agent.
- Dosages used for the CRI are given at sub-anesthetic levels so none of the dissociative effects are seen during CRI administration.
- Starting a ketamine CRI prior to a painful stimulus will provide the best means of preventing CNS sensitization but it is still effective in patient's that present with established pain.
- Loading dosage: 0.5mg/kg IV of ketamine should be given prior to starting the CRI in order to achieve initial therapeutic blood levels. Induction with ketamine/diazepam or Telazol® will provide an effective loading dose.
- CRI rate (intra-op): 10-20mcg/kg/min

- CRI rate (post-op): 2-10mcg/kg/min for at least 24 hours

Lidocaine (20mg/mL)
- MAC sparing and analgesic effects when administered as a CRI intra-op.
- Classified as a sodium channel blocker and a class IB antiarrhythmic.
- Displays free radial scavenging effects which may be helpful at preventing reperfusion injury.
- Acts as an inflammatory modulator by decreasing neutrophil chemotaxis and platelet aggregation.
- Acts as a prokinetic that enhances gut motility and helps prevent ileus.
- NOT recommended for use in cats due to its potential for toxicity. If used, do not exceed a dosage of 10mcg/kg/min and monitor closely for seizure activity and bradycardia.
- Commonly used as a first line treatment for ventricular premature complexes (VPC) or ventricular tachycardia.
- Some brands of lidocaine are sensitive to light. If lidocaine comes in a brown bottle the syringe or fluid bag containing the lidocaine should be covered when used as a CRI long term.
- Loading dosage: 1-2mg/kg IV of lidocaine should be given prior to starting the CRI in order to achieve an appropriate therapeutic level.
- CRI rate: 25-75mcg/kg/min

Dexmedetomidine (500mcg/mL or 100mcg/mL)
- Generally combined with an opioid CRI to enhance analgesia and sedation when an opioid CRI alone is not enough.
- Will greatly reduce MAC of inhalants when used intra-operatively.
- Commonly used during the post-operative period as a treatment for emergence delirium or when the patient would benefit from long term sedation during the post-operative period.
- Can be given in combination with ketamine, lidocaine and opioids
- Cardiovascular effects (significant bradycardia, biphasic effects on blood pressure) will likely be seen during CRI administration. Vital signs should be monitored closely. It is best to avoid a dexmedetomidine CRI if the patient has cardiovascular disease.
- Inhibits antidiuretic hormone (ADH) so an increase in urine production may be seen. The bladder should be expressed prior to recovery if used as an intra-operative CRI.
- Inhibits insulin release so a transitory hyperglycemia may be seen. Avoid a dexmedetomidine CRI if serial glucose values need to be obtained.
- Loading dosage: 0.5-1mcg/kg IV should be given prior to starting the CRI in order to achieve an appropriate therapeutic level.
- CRI rate: 0.5-3mcg/kg/hr

Medetomidine
- Used in the same manner as dexmedetomidine.
- Loading dosage: 1-2mcg/kg IV prior to starting the CRI.
- CRI rate: 1-2mcg/kg/hr

TABLE 1: Dosages for constant rate infusions (CRIs) used in CATS.

Drug	Loading Dose	CRI dose	Quick Calculation	Comments
Morphine (M)*	0.10 mg/kg IM	0.03 mg/kg/hr (0.5 mic/kg/min)	Add 15 mg to 500 ml fluid & run at 1 ml/kg/hr	Cat may need light sedation; can be combined with K &/or L
Hydromorphone (H)	0.025 mg/kg IV	0.01 mg/kg/hr	Add 5 mg to 500 ml fluid & run at 1 ml/kg/hr	May cause hyperthermia; can be combined with K &/or L
Fentanyl (F)	0.001-0.003 mg/kg IM or IV (1-3 mic/kg IV)	2-5 mic/kg/h (0.03-0.08 mic/ kg/m)post-op 5-20 mic/kg/h (0.08-0.3 mic/ kg/m intra-op	For 5 mic/kg/h, add 2.5 mg to 500 ml fluid & run at 1 ml/kg/hr	2.5 mg=50 ml F, remove 50 ml LRS before adding F; can be combined with K &/or L.
Methadone	0.1-0.2 mg/kg IV	0.12 mg/kg/hr	Add 60 mg to 500 ml fluid & run at 1 ml/kg/hr	MAY cause sedation; can be combined with K &/or L.
Butorphanol	0.1 mg/kg IV	0.1-0.2 mg/kg/hr	Add 50 mg to 500 ml fluid & run at 1 ml/kg/hr for 0.1 mg/kg/hr	Only moderately potent & has ceiling effect - use as part of multimodal protocol
Ketamine (K)*	0.25 mg/kg IV	0.12-0.6 mg/kg/hr (2 -10 mic/kg/ min)	Add 60 mg to 500 ml fluid & run at 1 ml/kg/hr for 0.12 mg/kg/hr	Generally combined with opioids; may cause dysphoria
Lidocaine (L)	0.25 mg/kg IV	1.5 mg/kg/hr (25 mic/kg/min) Some sources recommend no more than 10 mic/kg/min in cats	Add 750 mg to 500 ml fluid & run at 1 ml/kg/hr 10 mic/kg/min would be 300 mg lidocaine in 500 ml fluid with a rate of 1 ml/kg/hr	750 mg=37.5 ml, remove 37.5 ml LRS before adding L; can be combined with opioid &/or K; **Lidocaine MAY be contraindicated in the cat due to cardiovascular effects.**
Medetomidine (Med) or Dexmedetomidine (D)	1-5 mic/kg Med 1-2 mic/kg D Can be IV or IM May not be necessary	0.001-0.004 mg/kg/hr Med (1-4 mic/kg/hr) 0.0005-0.002 mg/kg/hr D	Add 500 mic Med or 250 mic D (0.5 ml of either) to 500 ml fluid and run 1-4 ml/kg/ hr	Provides analgesia and light sedation. Excellent addition to opioid CRI, or can be administered as solo drug CRI.
Morphine* / Ketamine*	M: 0.10 mg/kg IM K: 0.25 mg/kg IV	0.03 mg/kg/hr M & 0.12 mg/kg/hr K	Add 15 mg M & 60mg K to 500 ml fluid & run at 1 ml/kg/hr	Can be administered up to 3 ml/kg/hr but dysphoria MAY occur. Can substitute, F, or methadone for M.
Morphine / Ketamine / Lidocaine (MLK)	M: 0.10 mg/kg IM K: 0.25 mg/kg IV L: 0.25 mg/kg IV	0.03 mg/kg/hr M, 0.12 mg/kg/hr K; 1.5 mg/kg/hr L	Add 15 mg of M, 60 mg K and 750 mg (or 300 mg) L to 500 ml fluid & run at 1 ml/kg/hr	Can substitute H, F or methadone for M.

* Any of the drug amounts in the bag of fluids can be decreased and the fluids administered at a higher rate if necessary. For example, for morphine, ketamine and morphine/ketamine infusions, 7.5 mg of morphine & 30 mg of ketamine can be used and the CRI administered at 2 ml/kg/hr if more fluids are needed.

TABLE 2: Dosages for constant rate infusions (CRIs) used in DOGS.

Drug	Loading Dose	CRI dose	Quick Calculation	Comments
Morphine (M)*	0.5 mg/kg IM (or 0.25 mg/kg SLOWLY IV)	0.12-0.3 mg/kg/hr (2.0 mic/kg/min-3.3mic/kg/min	Add 60 mg to 500 ml fluid & run at 1 ml/kg/hr for 0.12 mg/kg/hr	MAY cause sedation; can be combined with K &/or L.
Hydromorphone (H)	0.05-0.1 mg/kg IV	0.01-0.05 mg/kg/hr	Add 5-24 mg to 500 ml fluid & run at 1 ml/kg/hr	MAY cause sedation; can be combined with K &/or L.
Fentanyl (F)	0.001-0.003 mg/kg IM or IV (1-3 mic/kg IV)	2-10 mic/kg/h (0.03-0.2 mic/ kg/m)post-op 3-40 mic/kg/h (0.05-0.7 mic/ kg/m intra-op	For 5 mic/kg/h, add 2.5 mg to 500 ml fluid & run at 1 ml/kg/hr	2.5 mg=50 ml F, remove 50 ml LRS before adding F; can be combined with K &/or L; Intra-op dose can be up to 20-40 mic/kg/h
Methadone	0.1-0.2 mg/kg IV	0.12 mg/kg/hr	Add 60 mg to 500 ml fluid & run at 1 ml/kg/hr	MAY cause sedation; can be combined with K &/or L.
Butorphanol	0.1 mg/kg IV	0.1-0.2 mg/kg/hr	Add 50 mg to 500 ml fluid & run at 1 ml/kg/hr for 0.1 mg/kg/hr	Only moderately potent & has ceiling effect - use as part of multimodal protocol
Ketamine (K)*	0.25 mg/kg IV	0.12-0.6 mg/kg/hr (2 -10 mic/kg/ min)	Add 60 mg to 500 ml fluid & run at 1 ml/kg/hr for 0.12 mg/kg/hr	Generally combined with opioids; may cause dysphoria; post-op dose may be higher
Lidocaine (L)	0.5 – 1.0 mg/kg IV	1.5-3.0 mg/kg/hr (25-50 mic/kg/min)	Add 750 mg to 500 ml fluid & run at 1 ml/kg/hr for 25 mic/ kg/min	750 mg=37.5 ml, remove 37.5 ml LRS before adding L; can be combined with opioid &/or K.
Medetomidine (Med) or Dexmedetomidine (D)	1-5 mic/kg Med 1-2 mic/kg D Can be IV or IM May not be necessary	0.001-0.004 mg/kg/hr Med (1-4 mic/kg/hr) 0.0005-0.002 mg/kg/hr D	Add 500 mic Med or 250 mic D (0.5 ml of either) to 500 ml fluid and run 1-4 mls/kg/hr	Provides analgesia and light sedation. Excellent addition to opioid CRI, or can be administered as solo drug CRI.
Morphine* / Ketamine*	M: 0.5 mg/kg IM K: 0.25 mg/kg IV	0.12 mg/kg/hr M & 0.12 mg/kg/hr K	Add 60mg M & 60mg K to 500 ml fluid & run at 1 ml/kg/hr	Can be administered up to 3 ml/kg/hr but sedation or dysphoria MAY occur. Can substitute H, F or methadone for M
Morphine / Ketamine / Lidocaine (MLK)	M: 0.5 mg/kg IM K: 0.25 mg/kg IV L: 0.5 mg/kg IV	0.12 mg/kg/hr M, 0.12 mg/kg/hr K; 1.5 mg/kg/hr L	Add 60 mg of M, 60 mg K and 750 mg L to 500 ml fluid & run at 1 ml/kg/hr	Can substitute H, F or methadone for M. Dr. Muir's dose is 3.3 mic/kg/min M, 50 mic/kg/min L; 10 mic/kg/min K.

*Any of the drug amounts in the bag of fluids can be decreased and the fluids administered at a higher rate if necessary. For example, for morphine, ketamine and morphine/ketamine infusions, 30 mg of morphine & 30 mg of ketamine can be used and the CRI administered at 2 ml/kg/hr if more fluids are needed.