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Review

# Current Topics in Marmoset Anesthesia and Analgesia

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## Abstract

Anesthetic and analgesics are essential components of both clinical and research procedures completed in marmosets. A review of current anesthetic and analgesic regimens for marmosets has been complied to provide a concise reference for veterinarians and investigator teams. Published dose regimens for injectable and inhalant anesthetic drugs and analgesic drugs are included. Appropriate physiological monitoring is key to the success of the procedure and perianesthetic options are provided. Although recent publications have refined anesthesia and analgesia practices, our review demonstrates the continued need for evidence-based resources specific to marmosets.

**Key words:** analgesia, anesthesia, marmoset, pain, sedation

## INTRODUCTION

The increased use of marmosets as a biomedical research model has required refinement of anesthesia and analgesia practices to facilitate optimal clinical care and research support. The marmoset's unique physiology and small size make drug selection challenging. Moreover, limited evidence-based literature further complicates decisions. We have compiled a thorough review of current anesthetic and analgesic regimens for marmosets to provide a concise reference for veterinarians and investigator teams. This resource also demonstrates areas that need continued evidence-based practice evaluation.

## SEDATION AND ANESTHESIA

Clinical and research procedures require varying degrees of tranquilization, sedation, or anesthesia to mitigate stress or pain associated with the procedure. Consideration of the degree of stress or pain induced by a procedure will allow selection of appropriate drugs and doses. The effects of drugs are typically dose dependent, and an understanding of terminology to describe the dose-dependent effect on the animal is helpful. Tranquilization, a reduction in anxiety without central depression, is less commonly used in nonhuman primates (NHP) as this does not facilitate safe handling. Sedation is central nervous system depression and relaxation, but patients may be responsive to noxious stimuli.[1] Sedation is often appropriate for less invasive procedures given the marmosets' small size and lack of serious zoonotic hazards. Dissociative sedation or anesthesia is commonly used in NHP. The dissociation of the thalamocortic and limbic systems produces analgesia and amnesia without a loss of consciousness, so general anesthesia is not achieved.[1,2] Anesthesia is the "loss of sensation to the entire or any part of the body."[1] General anesthesia refers to unconsciousness achieved through reversible depression of the central nervous system.[1] Different depths of anesthesia are selected based on the degree of invasiveness of a procedure. A surgical plane of anesthesia is the deepest state of anesthesia used and facilitates general surgery.[1]

Unique marmoset anatomy and physiology make anesthesia provision and maintenance challenging. Anatomy challenges revolve around the marmoset's small size. Small muscle masses limit the volume of drug that may be administered by injection,

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**Table 1** Substance Administration Routes and Volumes

| Substance Administration Route | Volume |
|---|---|
| Subcutaneous | Up to 20–30 mL/kg total with maximum 10 mL per site |
| Intramuscular | 0.25 mL/kg ideal with maximum 0.5 mL/kg per site[43] |
| Intravenous | Up to 10 mL/kg over 10 minutes[43]; 5 mL/kg or less can be infused at faster rates[45] |

especially drugs with a low pH such as ketamine that may cause myotoxicity.[3] A small oral cavity and the sharp angle of the larynx entering the trachea make intubation challenging.[4] An average tidal volume of 5 to 7 mL requires anesthetic systems and ventilation tubes with reduced dead space and caution when providing positive-pressure ventilation.[5] The high surface area to body mass ratio makes marmosets susceptible to heat loss and hypothermia when sedated or anesthetized; hypothermia and low blood pressure impair drug metabolism. Physiological challenges include an elevated metabolic rate that may impact drug metabolism.[6] Heart rates of 200–400 beats per minute (BPM) require monitoring equipment capable of detecting high heart rates.

## Injectable Sedation and Anesthetic Drugs

Injectable sedation and anesthesia regimens are commonly used for procedures lasting less than 30 minutes and for procedures of prolonged duration where inhalants may not be appropriate. Injections can be given via the intravenous (IV), intramuscular (IM), or subcutaneous (SC) routes. The quadriceps muscle is the largest muscle mass and most commonly used for IM injections; the vena saphena and lateral tail vein are used for IV injections in conscious or unconscious marmosets.[6] Suggested maximum volumes are provided in Table 1. The majority of injectable anesthetic regimens are dose dependent, and a higher dose will likely be associated with a deeper anesthesia of longer duration. However, a ceiling effect may limit the depth of anesthesia that can be achieved with a single drug. Variance in dose response may be seen between young (<2 years of age), adult (2–8 years of age), and aged (>8 years of age) marmosets. Comorbidities, such as dehydration and hypothermia, may impact drug effect and metabolism.

***N-Methyl-D-Aspartate (NMDA) Antagonists.*** Ketamine is a phencyclidine derivative that affects the thalamocortical and limbic systems through prevention of glutamate binding to receptors.[1] Ketamine has an advantageously wide safety margin. Doses of 5–50 mg/kg IM produce sedation or dissociative anesthesia, or are used for anesthesia induction.[6–10] A dose of 50 mg/kg IM yields 31.23 minutes of immobilization time and 135.84 minutes of recovery time (defined as time between lifting head and ability to safely ambulate in cage and be reunited with conspecific partner).[7] Ketamine alone provides adequate sedation for procedures with temporary pain, such as a blood draw, but is not sufficient for major surgery. Increased doses do not result in deeper levels of anesthesia, only increased duration of anesthesia or sedation when used as a single agent.[11] The low pH of ketamine formulations has led to myotoxicity and elevations in creatine kinase and aspartate transaminase.[3,7] Administration in large muscle groups, mainly the quadriceps, and limiting volume to no more than 0.1 mL per injection site can limit adverse reactions. Ketamine combined with alphaxalone (2.5 mg ketamine and 1 mg alphaxalone IM per marmoset) was found to produce lateral recumbency in 3 to 5 minutes, an average sedation time of 26.4 minutes, and recovery (defined as being able to return to their enclosure with a recovery score of 0) in an average 43.4 minutes.[12] Tiletamine is available as a combination product with zolazepam (Telazol, Zoetis; Parsippany, NJ); there are few reports of use in marmosets. The author (Goodroe) recommends a dose of 5–10 mg/kg to facilitate 20–30 minutes of sedation. Recovery is longer than ketamine, presumably due to slower metabolism of zolazepam.

***$\alpha_2$-Adrenergic Receptor Agonists.*** $\alpha_2$-Adrenergic receptor agonists, such as dexmedetomidine, medetomidine, and xylazine, bind to receptors throughout the body, producing sedation, muscle relaxation, analgesia, and effects on multiple organ systems. Cardiovascular effects include variance in systemic vascular resistance and blood pressure, heart rate, and rhythm (typically bradycardia), and an overall decrease in cardiac output. Respiratory effects are mild and may include a decreased respiratory rate. Hemoglobin oxygen saturation of peripheral capillaries ($SpO_2$) was found to decrease in conjunction with partial pressure of oxygen in arterial blood in marmosets administered ketamine 50 mg/kg, xylazine 2 mg/kg, and atropine 0.05 mg/kg IM.[13] Gastrointestinal motility may be decreased and urine production increased.[1] Solo use of $\alpha_2$-adrenergic receptor agonists in marmosets has not been reported and is unlikely to achieve sufficient sedation. Dexmedetomidine, medetomidine, and xylazine are often combined with ketamine to produce sedation or general anesthesia in marmosets. These combinations can achieve a deeper level of anesthesia, compatible with minor surgical procedures, and produce muscle relaxation. $\alpha_2$-Adrenergic receptor agonists can be reversed, facilitating a shorter anesthetic recovery time.

Several dose combinations of medetomidine and ketamine have been reported. Medetomidine 0.02 mg and ketamine 2 mg followed by atipamezole 0.1 mg IM facilitated brief restraint for fMRI placement and full recovery in less than 30 minutes.[14] Medetomidine 0.1 mg/kg and ketamine 3 mg/kg with atipamezole 0.5 mg/kg IM was used for brief procedures in a similar manner.[15] A reduced dose of medetomidine 0.05 mg/kg and ketamine 3 mg/kg IM has also been reported.[16] Medetomidine 0.5 mg/kg and ketamine 25 mg/kg IM resulted in prolonged recovery periods; marmosets displayed initial arousal and sat upright but were unable to be placed back safely in conspecific groups until 7 hours post injection despite administration of atipamezole 2.5 mg/kg IM. Reduction of medetomidine dose to 0.05 mg/kg and reversal with atipamezole 0.25 mg/kg IM resulted in recovery time of 5.25 hours.[7] Low doses of ketamine when used in combination with $\alpha_2$-adrenergic receptor agonists are recommended. A combination of alphaxalone (4 mg/kg), medetomidine (50 $\mu$g/kg), and butorphanol (0.3 mg/kg) administered IM produced lateral recumbency in 3 to 5 minutes, sedation for an average of 60.2 minutes, and recovery (defined as being able to return to their enclosure with a recovery score of 0) in an average of 57.5 minutes. There was no response to pressure applied to the tail at a maximum pressure of 200 mm Hg during the sedation period. When atipamezole (250 $\mu$g/kg) was given

IM 45 minutes after injectable sedation administration, recovery time was not significantly different; however, the incidence of vomiting during recovery was significantly reduced. It is recommended to be prepared to provide supplemental oxygen when using this protocol as severe bradypnea and hypothermia was observed in 1 marmoset. Caution should be used with geriatric marmosets or those with clinical concerns.[12]

Xylazine 1.5 mg/kg and ketamine 10–15 mg/kg IM are reported to provide good muscle relaxation.[16] There are no reports of dexmedetomidine use in marmosets, but the combination of dexmedetomidine 0.01 mg/kg and ketamine 10 mg/kg IM was evaluated in golden-headed lion tamarins. The dose was found to be safe and produced approximately 54–80 minutes of anesthesia; bradycardia, decreased respiratory rate, and muscle relaxation were noted.[17] The authors (Goodroe and Fitz) have used a similar regimen in marmosets with success.

Yohimbine and atipamezole are $\alpha_2$-adrenergic receptor antagonists that may be used to reverse the effects of $\alpha_2$-adrenergic receptor. Efficacy of medetomidine reversal with atipamezole administered IM in marmosets was not found to be sufficient.[7,12] IM administration of reversal agents is preferred to avoid hypotension associated with IV administration.[1]

***Benzodiazepines.*** Benzodiazepines enhance y-aminobutyric acid (GABA) binding to $GABA_A$ receptors, resulting in sedation and muscle relaxation.[1] Diazepam and midazolam are the most commonly used benzodiazepines; they are rarely used as sole sedation agents in marmosets. They are often combined with NMDA antagonists (ketamine) or in the combination product tiletamine and zolazepam (Telazol, Zoetis; Parsippany, NJ). There is minimal cardiovascular and respiratory depression.[1] Ishibashi and colleagues[18] found that a combination of midazolam 0.3 mg/kg, ketamine 10 mg/kg, and butorphanol 0.015 mg/kg IM followed by sevoflurane was a safe combination that produced balanced anesthesia in 271 of 273 marmosets with no anesthetic mortality. Furtado and colleagues[19] gave midazolam 1 mg/kg with approximately 10 mg/kg of ketamine IM and elicited 38.6 ± 31.5 minutes of immobilization. A combination of midazolam 0.2–0.4 mg/kg with ketamine 20–30 mg/kg IM is used by the author (Goodroe) for sedation prior to intubation or to perform dental extractions. Flumazenil is a benzodiazepine antagonist and can be used as a reversal agent (0.01–0.2 mg/kg IV)[1]; use in marmosets has not been reported.

***Propofol.*** Propofol is a $GABA_A$ receptor agonist, NMDA receptor antagonist, and glutamate antagonist.[6] IV administration provides a rapid onset and quick clearance. General anesthesia and muscle relaxation can be achieved with the use of propofol. There is no analgesia effect. Constant rate infusions may be appropriate for procedures when a quick recovery is ideal. The advantages of propofol to induce and maintain general or surgical anesthesia compared with inhalational anesthetics include lower risks of post operative nausea, vomiting,[20–23] and intraoperative hypotension;[24,25] precise control of anesthetic depth; ability to administer the anesthetic agent without a vaporizer; and no risk of environmental pollution and anesthetic exposure to the surrounding individuals.

Propofol is ideal as part of a balanced anesthesia regimen but requires endotracheal intubation due to apnea risk when used in combination with other anesthetic drugs or opioids. When propofol 8 mg/kg was administered IV at a rate of 4 mg/kg/min following administration of sevoflurane, apnea requiring intubation was observed in 2 of 6 marmosets. Administration of propofol 12 mg/kg at the same rate to marmosets without concurrent use of other anesthetics did not produce apnea. It is suggested that propofol in combination with other drugs may result in respiratory depression in marmosets; therefore, intubation and availability of ventilation support equipment are recommend.[26] Apnea is more common when propofol is administered quickly in other species.[1] The 12 mg/kg dose evaluated in marmosets resulted in an average of 5 minutes to onset, 5 minutes of sedation time, and 18 minutes for recovery. Heart rate decreased to 224–293 BPM and respirations decreased to 32–41 breaths per minute, both of which are clinically acceptable. Respiratory and heart rate decrease and recovery corresponded to sedation scores, consistent with drug metabolism.[26] Propofol 2–4 mg/kg IV provides sufficient muscle relaxation for endotracheal intubation when given after sedation with ketamine or a ketamine combination.[27] Propofol is an ideal component of surgical anesthesia for cesarean section due to rapid neonatal clearance; the concentration of inhalant anesthesia can often be reduced when propofol is given as a constant rate infusion (CRI) with inhalant anesthesia.[1]

***Alphaxalone.*** Alphaxalone is a GABA agonist steroid anesthetic.[28] Alphaxalone produces adequate muscle relaxation and may be used for both sedation and general anesthesia. Alphaxalone does not have analgesic effects.[29] Dose-dependent respiratory depression is observed in multiple species, but effects do not require intubation at commonly used dosages.[1] $SpO_2$ was found to decrease in conjunction with partial pressure of oxygen in arterial blood (50–70 mm Hg) in marmosets administered alphaxalone 12 mg/kg IM; no apnea was noted and respiratory rate was approximately 30 respirations per minute.[13] Bakker and colleagues found alphaxalone to elicit no excessive salivation or vomiting.[7] Administration of alphaxalone 15 mg/kg IM and measurement of blood pressure 10 and 30–40 minutes post injection found blood pressure was initially decreased, then increased, presumably as the drug was metabolized.[28] This correlates with reports of dose-dependent cardiovascular depression (measured as arterial blood pressure, cardiac output, and heart rate) observed in dogs and cats.[1] Myoclonic twitches are observed during recovery, and it is helpful to educate observers who may mistake these movements for seizures.[30]

Initial sedation to place an IV catheter can be achieved with alphaxalone 10 mg/kg IM, and subsequent 3 mg/kg IV can obtain sufficient muscle relaxation for endotracheal intubation.[4] Alphaxalone 12 mg/kg IM has a longer induction and sedation time with faster recovery time than ketamine 50 mg/kg IM. Average induction with alphaxalone was 2.54 minutes, which was 1.3 minutes longer than ketamine induction (1.24 minutes). Immobilization time (defined as time from loss of postural tonicity to first attempt to raise head) with alphaxalone was 53.72 minutes, which was 22.49 minutes longer than ketamine immobilization (31.23 minutes). Recovery time (defined as ability to walk and climb confidently in an enclosure) for alphaxalone was 55.79 minutes, which was 80.05 minutes faster than recovery from ketamine (135.84 minutes). Overall, recovery from alphaxalone was found to be more ideal then recovery from ketamine. There was less vocalization, salivation, and uncoordinated muscle activity.[7] Another evaluation of alphaxalone administered 12 mg/kg IM found a shorter duration of sedation (average 31.7 minutes, defined as onset to lateral

recumbency to first spontaneous movement) with a similar recovery time (average 62.5 minutes, recovery defined as being able to return to their enclosure with a recovery score of 0).[12] Both evaluations of alphaxalone 12 mg/kg IM included stimulation either by hind-limb withdrawal assessed via use of hemostats to apply pressure or pressure applied to the tail. The differences in sedation times may be due to variance in definitions of those times or inter-individual variance.[12] Alphaxalone 16 mg/kg IM has been used to complete short abdominal telemetry surgeries with meloxicam and buprenorphine administered for analgesia.[31] Administration of alphaxalone 16 mg/kg IV after premedication with buprenorphine, butorphanol, or tramadol has also been evaluated.[32] Apnea lasting 27 ± 18 minutes was noted in 8 of 9 marmosets receiving buprenorphine. Butorphanol elicited apnea (14 minutes) in 2 of 9 marmosets. Tramadol showed no anesthetic complications. There was no difference in quality of the recovery period, body weight, or food and water intake post anesthesia. The control marmosets that received only alphaxalone 16 mg/kg IV in this study exhibited 67.3 ± 26.5 minutes of immobilization followed by a recovery period of 43.8 ± 13.9 minutes.

A combination of alphaxalone 10 mg/kg IM and diazepam 0.3 mg/kg IM has been used to achieve approximately 30 minutes of immobilization or facilitate muscle relaxation sufficient for endotracheal intubation.[33,34] A combination of alphaxalone (4 mg/kg), medetomidine (50 μg/kg), and butorphanol (0.3 mg/kg) administered IM has already been described.[12]

### Constant Rate Infusions

Partial IV anesthesia (PIVA) is the IV administration of 1 or more drugs in addition to inhalants. Total IV anesthesia achieves anesthesia without the use of inhalants. PIVA and total IV anesthesia may provide a more balanced plane of anesthesia as lower doses of drugs may be used when in combination, and this may reduce individual drug adverse effects. Drug doses can be reduced to achieve various levels of sedation or anesthesia based on procedure requirements. These protocols may also be advantageous for research procedures that restrict which drugs may be used. Drugs can be administered IV as a bolus or as a CRI. Providing drugs as a CRI prevents variable levels of sedation associated with repeated IM dosing. Marmosets have a total blood volume of 20–35 mL of blood (70 mL/kg).[16] Total volumes infused, especially during longer procedures, must be considered. Total fluid rates of <5 mL/kg/h are advisable, but further reduction should be considered for longer procedures. Attention should be paid to urine production, hematocrit, and electrolyte levels to guide fluid volumes administered in long procedures. A fluid pump capable of administering small volumes over extended lengths of time is highly recommended to ensure appropriate dosing. Propofol administered at 0.6–1.0 mg/kg/min has been used to facilitate imaging. A lower propofol dose (0.3 mg/kg/min) can be used in conjunction with fentanyl (10–20 μg/kg/h).[35] An IV alphaxalone bolus of 2–5 mg/kg followed by a 0.17 mg/kg/min CRI facilitates imaging or surgery.[6] Sufentanil 8 μg/kg/h with nitrous oxide inhalant provides immobilization for neuroscience studies after initial induction with alphaxalone and diazepam.[36]

## Inhalant Anesthesia

Inhalant anesthetics are ideal for longer procedures and major surgeries due to quick adjustment of anesthetic depth via dose titration, ability to maintain a stable plane of anesthesia, reduced systemic absorption, and faster recovery to normal function.[1] Inhalant anesthetics produce reversible loss of consciousness, amnesia, and muscle relaxation. Sevoflurane and isoflurane are the only reported inhalants used in marmosets.[6,18,37] Our understanding of the mechanism of action is incomplete, but the interaction of inhalants with GABA receptors, potassium and sodium channels, muscarinic and nicotinic receptors, and NMDA receptors in the brain and spinal cord has been described; no single receptor is responsible for the clinical effects that occur, suggesting a combination of receptor interactions are likely responsible.[1] Adverse effects are dose dependent and include depressed respiratory rate and tidal volume, decreased cardiac output, decreased arterial blood pressure, and increased intracranial pressure.[1]

Inhalant anesthetics are administered via vaporization to the lungs through an endotracheal tube, face mask, or induction chamber. Minimum alveolar concentrations are not available, but 1%–4% isoflurane and 2%–5% sevoflurane have been recommended.[6] Endotracheal tubes are used to maintain an open airway and can create a closed system that facilitates control of the airway by use of positive-pressure ventilation as well as providing protection from regurgitated material entering the airway. Masks do not produce a complete seal of the airway, and animals may have variable anesthetic uptake depending on respiratory rate and volume. Custom printed masks may provide a better seal around the patient's face.[37] Induction chambers are used for marmosets, but inhalation of volatile anesthetics is associated with gastrointestinal upset and mucous membrane discomfort. Noxious odors cause a stress response. If induction chambers are used, the recommendation is not to prefill the induction box with anesthetic gas and increase in 1% increments every 30 to 60 seconds. Premedication with a low dose of injectable sedation (Table 2) is recommended for adult marmosets prior to use of an induction chamber.[6]

Use of a balanced anesthetic regimen featuring an initial injectable sedation regimen facilitates intubation. A protocol utilized by the authors (Goodroe and Fitz) consists of initial sedation with ketamine or ketamine with midazolam, placement of an IV catheter, and administration of propofol followed by endotracheal intubation and anesthesia maintenance with isoflurane. The small oral cavity and larynx make intubation challenging, and failed attempts can quickly lead to laryngeal inflammation that may require oxygen support and steroid administration. This can be ameliorated through using an appropriately sized laryngoscope (0 or 00 Miller blade) and adequate visualization. Use of gauze or string secured by the dentation can facilitate a wide opening of the oral cavity without close proximity of the holder's hands. Securing the tongue with atraumatic long forceps brings the larynx into visual alignment so that the arytenoids are easier to visualize. Lidocaine can be applied topically to the laryngeal cartilages to reduce muscle spasms. A stylet that extends approximately 90% of the endotracheal tube length may be helpful to overcome the angle of the larynx as it enters the trachea (137 ± 10 degrees) and large portion of the tongue in the hypopharynx. Use of a tilting stand has been described that secures the marmoset's head to allow visualization of the larynx and eliminate the need for an assistant.[4]

The distance from the nose to the tracheal bifurcation is 8.1 ± 0.5 cm.[4] The endotracheal tube length should be measured for each patient and the tube marked so any tube movement can be easily identified during procedure manipulations. The trachea diameter is 4.8 ± 0.2 mm at the third tracheal ring.[4] This

**Table 2** Injectable Sedation and Anesthetic Regimens

| Drug | Dose | Notes |
|---|---|---|
| Alphaxalone | 5–7 mg/kg IM | Sedation[27] |
| | 7–15 mg/kg IM | Immobilization 30–60 min[7,12,13] |
| | 16 mg/kg IM | Abdominal implantation surgery[31] |
| | 10–12 mg/kg IM followed by 3 mg/kg IV | Endotracheal intubation[4] |
| | 16 mg/kg IV | Immobilization 30–90 min[32] |
| | 10 mg/kg with diazepam 0.3 mg/kg IM | Endotracheal intubation; immobilization 30 min[33,34] |
| | 18 mg/kg with diazepam 0.05 mg per animal IM | [33] |
| | 1 mg per animal with ketamine 2.5 mg per animal IM | Immobilization 20–30 min[12] |
| | 4–10 mg/kg with ketamine 20–30 mg/kg IM | [27] |
| | 4 mg/kg with medetomidine 50 $\mu$g/kg and butorphanol 0.3 mg/kg IM | Immobilization 60 min[12] |
| | 10 mg/kg with diazepam 3 mg/kg and atropine 0.2 mg/kg IM, followed by sufentanil 8 $\mu$g/kg/h IV with nitrous oxide inhalant | Surgical anesthesia induction and CRI for auditory physiology[36] |
| Ketamine | 15–20 mg/kg IM | Light sedation[6,8–10] |
| | 20–40 mg/kg IM | Sedation, induction of anesthesia[6,8,18] |
| | 40–50 mg/kg IM | General anesthesia, 30 min immobilization[6,7] |
| | 10–30 mg/kg with midazolam 0.2–0.4 mg/kg IM | Sedation prior to intubation, sufficient for dental extractions[27] |
| | 10 mg/kg with midazolam 1 mg/kg IM | Approximately 30 min of immobilization[19] |
| | 10 mg/kg with midazolam 0.3 mg/kg and butorphanol 0.015 mg/kg IM | Induction of anesthesia[18] |
| | 10 mg/kg with dexmedetomidine 0.02–0.03 mg/kg IM | Sufficient sedation for short dental procedure[27] |
| | 3 mg/kg with medetomidine 0.05–0.1 mg/kg and atipamezole 0.5 mg/kg IM | Brief restraint to place into imaging system (fMRI)[14–16] |
| | 50 mg/kg with xylazine 2 mg/kg and atropine 0.05 mg/kg IM | 60–90 min immobilization[13] |
| | 10–22 mg/kg with xylazine 1–1.5 mg/kg IM | Muscle relaxation facilitates intubation[9,16] |
| Propofol | 2–4 mg/kg IV | Bolus to facilitate intubation[9,27] |
| | 12 mg/kg IV | 5 min of sedation[26] |
| | 0.3–0.5 mg/kg/min IV | CRI[9] |
| | 0.3 mg/kg/min with fentanyl 10–20 $\mu$g/kg/h IV | Imaging CRI (animal intubated)[35] |
| | 0.6–1.0 mg/kg/min IV | Imaging CRI (animal intubated)[35] |
| Tiletamine/ zolazepam (Telazol) | 5 mg/kg IM | 15 min of sedation[9,47] |
| | 5–10 mg/kg IM | 20–30 min of sedation |

facilitates placement of a 2-mm endotracheal tube; 1.5- or 1.0-mm tubes can be used for younger marmosets or those that are challenging to intubate. It is recommended to use the largest endotracheal tube that will fit to provide the largest patent airway feasible. When using small-diameter endotracheal tubes, be aware that they are prone to developing kinks and certain materials such as silicone may kink more easily. Once a kink develops in a tube, it is more likely to reoccur; it is ideal to discard tubes that kink and not consider reuse. Larger endotracheal tubes are often made of a thicker material that is less likely to kink and obstruct air delivery. Careful monitoring of respirations is important to identify an endotracheal tube kink that may occur and occlude the lumen. The weight of the breathing circuit tubing must be considered to avoid excess pull on the endotracheal tubing. Use of an anesthesia breathing circuit support or tube tree placed close to the patient will help alleviate any excess pull. Tape may also be used to secure the breathing circuit but must be removed if there is any patient movement to avoid extubation. When using a stereotaxic device, the anesthetist should closely observe the endotracheal tube anytime the patient is manipulated to ensure no tube movement or kinks develop. Many devices include a support bar that contacts the upper palate, and care must be taken to ensure the endotracheal tube is not occluded by this device. Adequate padding should be placed under the marmoset to ensure the angle of the neck relative to the head and body is not too sharp in order to avoid both muscle soreness and ensure a patent airway.

A marmosets' tidal volume is 5 to 7 mL. This small volume requires use of a non-rebreathing system (ex. Bain or Modified Jackson Rees systems) to ensure they do not rebreathe the air they exhaled. Positive-pressure ventilation can be provided through the use of a circuit block or a ventilator. A ventilator capable of small-volume gas delivery, such as the Hallowell Anesthesia WorkStation (000A2770 Anesthesia WorkStation, Hallowell, Pittsfield, MA), is required.

Disadvantages of inhalational anesthetics include the need for specialized equipment with routine maintenance requirements and risk of environmental pollution with anesthetic exposure to the surrounding individuals. Dose-dependent respiratory rate depression and decreased cardiac output occur.[1] Isoflurane

**Table 3** Analgesic Regimens

| Drug | Dose | Notes |
|---|---|---|
| Acetaminophen | 6 mg/kg PO q12–24 h | [27] |
| Bupivacaine | 1–2 mg/kg | Local infiltration block[27] |
| Buprenorphine | 0.005–0.02 mg/kg IM q6–8 h | Dosing frequency based on 0.02 mg/kg dose[9,32,49]; recommend low dose if given in conjunction with anesthesia |
| Buprenorphine SR | 0.1–0.2 mg/kg SC q3–3.5 d | [27,49] |
| Butorphanol | 0.02–0.2 mg/kg IM | [9,32] |
| Carprofen | 2.2–4.4 mg/kg PO q12–24 h | [27] |
| Ketoprofen | 2–5 mg/kg SC q12–24 h | [27] |
| Lidocaine | 2–4 mg/kg | Local infiltration block[27] |
| Meloxicam | 0.1–0.2 mg/kg q24 h SC, IM, PO | [16,27] |
| Meloxicam SR | 0.6 mg/kg SC | [27] |
| Oxymorphone | 0.075 mg/kg IM, q4–6 hours | [47] |
| Tramadol | 1.5 mg/kg IM | [32] |

was recently shown to decrease interhemispheric and thalamic functional connectivity of resting-state networks.[38]

## PHYSIOLOGICAL MONITORING OF MARMOSETS

### Heart Rate

Monitoring heart rate requires equipment capable of detecting high rates (at least 350 BPM) in small animals. Marmosets have been found to have a heart rate of 230 ± 26 BPM measured via telemetry in unrestrained marmosets (Table 4). Increase of heart rate in response to restraint, even when accustomed to the apparatus, elicited a heart rate increase from 230 to 348 BPM.[39] Heart rate and mean arterial pressures (MAPs) exhibit diurnal patterns with an additional decrease at midday.[39] Evaluation of heart rates under injectable sedation found the following: ketamine 370 BPM, alphaxalone 320 BPM, ketamine and medetomidine 230 to 260 BPM.[7] Electrocardiograms can be obtained with probes designed for pediatrics or rodent use.

### Hemoglobin Oxygen Saturation

$SpO_2$ is a less invasive, surrogate measurement of hemoglobin oxygen saturation of arterial blood and partial pressure of oxygen in arterial blood.[1] Measurement requires sensors that can be secured to the marmoset's small digits; sensors may be attached to a clip or adhesive. Sensors designed for pediatric use or rodents are helpful. Measurements are obtainable with the clips attached to palmer and planter surfaces or a shaved forearm. If adequate signals are not detected with sensor clips, adhesive sensors may place less pressure on the vessel and result in a better signal.

The following monitors have been reported to work on marmosets: Nonin 8600FO (Nonin Medical, Inc., Plymouth, MN), DRE Waveline EZ Portable Veterinary monitor (DRE Veterinary, Avante Company; Louisville, KY), System Vetrends 6400 (Vet TRENDS; Tampa, FL),[6] Ohmeda Biox 3740 (BOX Health Care, Inc.; Louisville, KY),[7] Advisor 3 Parameter Vital Signs Monitor with Universal "Y" Sensor (V1703) and reflectance sensor (V1700) (Surgivet, Smiths Medical; Dublin, OH),[37] Covidien PM10N with disposable $SPO_2$ sensor N25 (Covidien; Dublin, Ireland),[13] and Sentinel-V TidalGard S/SC (Leading Edge Veterinary Equipment; Centennial, CO).

### Blood Pressure

A MAP of 90–95 mmHg has been reported via telemetry unit.[39,40] Blood pressure has been shown to increase with handling; MAP 107 ± 16 mmHg via arterial catheter and MAP 96 ± 6 mmHg with tail cuff in restrained marmosets.[39]

A protocol for non-invasive blood pressure in non-sedated restrained marmosets was created by Mietsch and Einspanier. The thigh was the best measurement location for high-definition oscillometry in awake marmosets (VET HDO Monitor MD PRO Marmoset; S+B medVET GmbH, Babenhausen, Germany with C2 and V2 cuffs). A cuff width to leg circumference ratio of 30%–40% and acclimatization period of 1–3 minutes is recommended before taking measurements. The first measurement should not be used and an additional 3–5 collected with the mean calculated. The authors found means of 98.3 0.46 mmHg (MAP), 145.7 ± 9.0 mmHg (systolic arterial pressure), and 72.6 ± 6.44 mm Hg (diastolic arterial pressure).[41] Ultrasonic Doppler probes with size 1 and 2 neonatal cuffs encircling the tail are a reliable way to obtain systolic arterial pressure.[6]

The effect of injectable anesthetics on MAP was evaluated: ketamine 90 mmHg MAP, alphaxalone 95 mmHg MAP, and ketamine and medetomidine 70–90 mmHg MAP.[7] Ansel et al evaluated blood pressure in marmosets sedated with alphaxalone 15 mg/kg IM with the CODA Surgical Monitor (Kent Scientific; Torrington, CT). This monitor uses a volumetric tail cuff to determine MAP. MAP was 69.9 ± 4.1 mmHg 10–15 minutes after injection and 98.8 ± 16.8 mmHg 30–45 minutes after injection.[28]

Additional equipment used in marmosets includes: PhysioTel Telemetry System with telemetry transmitter (TA11PAC40) (Data Sciences International; St. Paul, MN);[39,42] vetHDO monitor with MDSoftware with CriticonWSoft-cufW, size: I (S+B medVET GmbH; Babenhausen, Germany);[7] OMRON HEM-608 (Omron Healthcare, Inc.; Vernon Hills, IL).[13]

### Temperature

Normal body temperature during daytime hours is 101.1–102.4°F (38.4–39.1°C) (Table 4).[9] A suggested goal is to maintain a rectal temperature of 100–101 F (37.8–38.3°C) during anesthesia.[6] The large body surface area relative to body mass makes temperature regulation during anesthesia challenging. A direct effect between length of immobilization period and body temperature decline has been observed.[19,32] Temperature decreased 37.4°F

**Table 4** Normal Physiologic Parameters

| Parameter | Normal Value |
|---|---|
| Heart rate | Unrestrained: 230 ± 26 beats/min[39]<br>Restrained: 348 ± 51 beats/min[39] |
| Respiratory rate | 36–44 breaths/min[9] |
| Temperature | 101.1–102.4°F (38.4–39.1°C)[9] |

(3°C) after 20 minutes of sedation when external heat support was not provided.[7]

Thermal support can be provided and controlled via electrical heat mats and warm air or water recirculating devices (eg, Bair Hugger System [3M; St. Paul, MN], HotDog Patient Warming Systems [Eden Prairie, MN]). Post procedure, intensive care units can be used to provide more complete thermal support (Perupa, P-100, Tokyo Menix; Japan).[13] Avian brooders are also an option for providing thermal support (RCM MX-BL 500 N Large Avian Brooder Nursery ICU; R-Com, Korea). Temperature of fluids administered IV should be closely monitored and controlled (eg, enFlow IV Fluid and Blood Warming System [Vital Signs, Inc. a GE Healthcare Company; Lexington, KY]). Marmosets can be overheated quickly when thermal support is provided, and rectal temperature should be closely monitored.[43] Heat lamps or infrared heaters provide supplemental heat for marmosets in their home enclosures; care should be taken to secure cords out of animal reach and direct heater so that distinct thermal zones are available to the marmoset.[6] Infrared heaters are advantageous since they do not heat metal, a common material for enclosures and nest boxes.

## Respiratory Rate

Normal respiratory rate per minute (RR) is 36–44 (Table 4).[9] Marmosets sedated with ketamine had a slightly higher RR, approximately 60.[7] Ketamine, xylazine, and atropine elicited a RR of 47 ± 8.25, and RR post alphaxalone administration was 27.33 ± 7.10.[13] Monitoring rate can be achieved through direct observation of chest movements (may not be possible under surgical drapes), reservoir bag movement, pressure gauge movements (some gauges may not be sensitive enough to detect changes), or end tidal carbon dioxide wave forms.

## End Tidal Carbon Dioxide

Exhaled carbon dioxide measured by a capnograph provides an assessment of alveolar ventilation and helps guide respiratory support during anesthetic events. Given the small tidal volume exhaled by marmosets, accurate measurements are difficult, but through use of small airway adapters, samples can be obtained to facilitate waveform evaluation (time capnography). Mainstream capnometers add deadspace and resistance to the breathing circuit; side stream capnometers are recommended for small animals, but delays in output secondary to small tidal volumes may be noted.[1]

## Muscle Relaxation and Reflexes

The pedal withdrawal reflex is an indicator of both depth of anesthesia and analgesia; testing with hemostats or a firm pinch to the digits of the hind limbs has been described in marmosets.[32] The palpebral reflex can aid in assessment of sedation level, but absence does not indicate adequate depth of anesthesia for invasive or painful procedures. Bakker et al[7] provides a scoring system for these reflexes that can be applied to clinical evaluations. Lack of jaw tone is a useful adjunct assessment of adequate anesthesia level in animals that are intubated.

## Fluid Support

Blood volume in a marmoset is approximately 70 mL/kg.[16] An isotonic electrolyte solution is usually provided SC or IV when marmosets are sedated for longer periods of time (>30 minutes). Intra-anesthetic fluid therapy supports normal cardiovascular function and counters negative effects of anesthetic agents (hypotension, bradycardia, vasodilation).[44] SC fluids can be used for short procedures (<30 minutes) in healthy, hydrated marmosets. An amount of 30 mL/kg is a good starting point for SC fluid administration volume. The literature describes a maximum SC dosing volume of 5 mL/kg per site.[45] However, the authors (Goodroe, Fitz, Bakker) find that marmosets weighing greater than 350 g have adequate loose skin around the dorsal thorax that allows administration of up to 10 mL in 1 location. During SC fluid administration, care should be taken to palpate the skin to ensure fluid accumulation does not lead to inappropriate tension. For clinically ill marmosets, especially those that are dehydrated or for procedures lasting longer than 30 minutes, consider IV fluid administration. A 22- to 26-gauge catheter can be placed in the saphenous, cephalic, or lateral tail vein;[4] 3–5 mL/kg/h IV is adequate for healthy marmosets.[6,44] Marmosets with dehydration requiring anesthesia should be clinically evaluated prior to devising a fluid therapy plan that provides for replacement and maintenance fluids. For long anesthetic procedures, consider decreasing the fluid rate by 25% after the first hour if the patient is stable.[44] Infusion rate can be precisely monitored with a fluid pump. The bladder should be evaluated periodically during long procedures, especially when fluids are being administered. The bladder can be gently expressed manually to ensure distension does not occur. Additional monitoring considerations that may influence rate and type of fluids provided include packed cell volume, blood pressure, glucose, and electrolytes.[6]

## Pre-anesthetic Care

In general, marmosets are fasted 6–12 hours prior to induction of general anesthesia.[46,47] For short sedations under injectable anesthesia, removal of food 1–2 hours prior to sedation is usually sufficient. Unexpected events warranting immediate anesthesia can be completed with care without fasting. Consider use of maropitant (1 mg/kg SC q24h) or ondansetron (0.2 mg/kg IM q24h) to aid with nausea and decrease risk of aspiration.

Pre-anesthetic evaluation should be considered based on type and length of procedure and condition of the animal. Evaluations can be as simple as a cage side observation or consist of an exam with bloodwork. i-STAT 1 and i-STAT Alinity v (Abaxis North America; Union City, CA) are point of care systems that use low blood volumes (approximately 0.2 mL) and have blood gas and chemistry cartridges available.[6]

## Post Anesthetic Care

Separation from social groups may be stressful for marmosets; if marmosets undergoing post anesthetic monitoring require individual housing to facilitate treatments, consider maintaining them within visual and olfactory contact of their group.[48]

Scoring systems for general appearance, locomotor activity, respiration, feces and urine production, and food intake are described.[31] These systems can be modified to meet institutional needs and serve to provide consistent language for all staff to use. Bodyweight is a good indicator of return to normal function;

loss may be associated with failure to consume diet as usual.[7] Care should be taken to ensure marmosets resume normal dietary intake and are provided supplemental care as needed. It is best not to deviate from the animal's normal diet, but in the immediate post anesthetic period additional supplemental food may be needed to ensure adequate caloric intake. Mixing the regular diet with a sweet liquid or increased serving sizes of favored enrichment items like gum Arabic are common supplements. Hypothermia can be ameliorated with cage side heat lamps or radiant heaters, but severe hypothermia may require use of an incubator.

## ANALGESIA

Analgesia it the "absence of pain in response to stimulation which would normally be painful" in a conscious animal.[1] Only 1 publication regarding pharmacokinetic profiles of an analgesic in marmosets is available (Fitz et al[49]). There is no other information regarding efficacy or pharmacokinetics, and analgesic doses are extrapolated from other species. When developing an analgesic plan, the impact on research, route, and frequency of administration and type of pain should all be considered. A multimodal approach to pain management using drugs of various methods of action is ideal (Table 3).

### Opioids

Opioids interact with 3 receptors: mu, kappa, and delta. Full agonists yield dose-dependent effects while partial agonists plateau at a lesser effect. Opioid receptors are widespread, resulting in many systematic effects aside from analgesia. Some common effects include sedation, mild respiratory depression, mild bradycardia, emetic or antiemetic effects, and decreased gastrointestinal motility. Variations of the mu receptor lead to species-specific sensitivity to adverse effects. First-pass metabolism results in low oral bioavailability and common administration routes are IV, IM, or SC. Opioids are most effective at decreasing pain transmitted by C-fiber nociceptors and are best combined with non-steroidal anti-inflammatory drugs (NSAIDs) for surgical procedures that may also elicit pain from A-$\beta$ fibers.[1] Naloxone is an antagonist that can be used to reverse opioids. Opioids have been shown to reduce the minimum alveolar anesthetic concentration (MAC) of inhalant anesthetics in many species, but effect on NHP has not been formally evaluated.[50–52]

Buprenorphine is a partial mu agonist and kappa antagonist.[53] It is a favored analgesia treatment due to its longer duration of action compared with other opioids. Analgesiometric assays and comparative studies have been completed in rats, rabbits, dogs, cats, sheep, pigs, and humans with favorable results. There is a "ceiling effect" at which higher doses of buprenorphine will not elicit additional analgesia.[53] Although side effects such as respiratory depression, nausea, or constipation have been described for morphine and its derivatives, none of these adverse effects were observed in a large cohort of unsedated rhesus monkeys that received treatment doses increasing from 20 $\mu$g to 100 $\mu$g/kg IM.[54]

Buprenorphine has been administered at 0.005–0.02 mg/kg IM or SC to marmosets every 6–12 hours. Buprenorphine is available in a 0.3-mg/mL concentration; this requires dilution to 0.03 mg/mL to facilitate administration.[37] Diluted buprenorphine in bacteriostatic 0.9% saline retains 90% of its initial concentration for up to 180 days when stored in glass vials in the dark or refrigerated; concentration declines rapidly when stored in plastic syringes.[55] A recent pharmacokinetic study suggests that a 12-hour administration frequency is inadequate. Fitz et al.[49] demonstrated that buprenorphine 0.02 mg/kg IM exceeds therapeutic levels (0.1 ng/mL in plasma) 5 minutes post injection and recommended a dosing frequency of 6–8 hours. This suggests that lower doses often utilized in practice may require more frequent administration. This study also confirmed variation in buprenorphine plasma levels among individuals, emphasizing the need for individual animal assessments to ensure adequate analgesia. The lipophilic nature of the drug results in differences among individuals with different body compositions. Opioids are often protein bound and are eliminated by hepatic mechanisms with varied enzyme activity, making dose extrapolation across species difficult.[1]

Respiratory depression and apnea are common adverse effects associated with buprenorphine administered concomitantly with anesthetics. Respiratory depression has been associated with the mu opioid receptor; the marmoset's sensitivity to respiratory depression may be secondary to a unique mu receptor subtype. Opioid binding sites differ in binding affinity and capacity between marmosets and rats.[56] Buprenorphine 0.03 mg/kg SC given after administration of ketamine 15–20 mg/kg IM required artificial ventilation and led to several deaths.[57] Buprenorphine 0.02 mg/kg IM given 60 minutes prior to anesthesia with alphaxalone 16 mg/kg IV led to 27 $\pm$ 18 minutes of apnea in 8 of 9 marmosets. Apnea occurred within 2–5 minutes of alphaxalone administration. Treatment with supplemental oxygen and manual chest compressions was successful.[32] Additional treatments for opioid-induced apnea include naloxone and stimulation of GV26 acupuncture point on the nasal plenum. Naloxone is an opioid antagonist and can be administered at 0.1–0.2 mg IV with repeated doses as needed.[47] The repeated finding of respiratory depression and a slow recovery has shaped the administration of buprenorphine at most institutions to only after spontaneous ventilation has been noted during recovery from anesthesia.

Buprenorphine SR (Zoopharm; Fort Collins, CO), a sustained-release formulation of buprenorphine, has been given at doses of 0.12–0.2 mg/kg SC both pre-operatively and post operatively with no reports of significant respiratory depression in marmosets. Fitz et. al[49] demonstrated that buprenorphine SR exceeds therapeutic levels (0.1 ng/mL in plasma) 15 minutes post injection and remained over the therapeutic level for 72 hours. A dosing interval of 3 to 3.5 days is recommended. Decreased animal handling for analgesia administration may result in a faster recovery and decreased animal stress. No injection site reactions were noted when buprenorphine SR was administered SC in the ventral abdomen. Mild decreased activity was noted. The authors (Goodroe, Fitz) have administered 0.1 mg/kg SC, and reduced impact on activity level was observed.

Epidural anesthesia consisting of buprenorphine 0.005 mg/kg and lidocaine 2 mg/kg with administered volume of 0.1–0.2 mL/kg in conjunction with isoflurane has been utilized by 1 of the authors (Fitz). The protocol resulted in balanced anesthesia during a cesarean section; isoflurane concentration to maintain a surgical plane of anesthesia was reduced to 0.5%–1%.

Oxymorphone, a full mu agonist, 0.075 mg/kg IM, q4–6 hours, has been used in marmosets.[47] No controlled studies have been conducted in marmosets, but titi monkeys administered 0.075 mg/kg IV maintained plasma therapeutic concentrations for 2 hours and a sedative effect was observed.[58]

Fentanyl, a full mu agonist, has a short duration of effect and is useful as a constant rate infusion to reduce the MAC of inhalant anesthesia required.[1] The authors have used a bolus of 1 $\mu$g/kg fentanyl followed by an IV CRI (1–20 $\mu$g/kg/h) during general anesthesia with isoflurane in 4 common marmosets. An amount of 15–20 $\mu$g/kg/h was associated with decreased RR. When 10 $\mu$g/kg/h was used in 2 marmosets undergoing terminal laparotomy, a reduced concentration of isoflurane was required to maintain surgical anesthesia. A 5-$\mu$g/kg IV CRI in conjunction with isoflurane in a surgical amputation resulted in a stable anesthetic plane and cardiorespiratory parameters throughout the surgical procedure, and the marmoset recovered without complication.

Butorphanol, a mu antagonist to partial agonist and kappa agonist, is used in the management of mild to moderate pain for short durations.[1] Administration at 0.2 mg/kg IM with alphaxalone led to apnea in 2 of 9 marmosets for 14 minutes.[32]

Tramadol HCl is a single-entity, centrally acting analgesic that is effective for the management of moderate to severe pain. It is metabolized to O-desmethyltramadol, which is a full mu agonist. Although the mechanism of action of this analgesic is not completely understood, animal models suggest that tramadol binds to the mu-opioid receptors and weakly inhibits norepinephrine and serotonin reuptake. Although still under debate, tramadol could be an effective analgesic that may have a particularly important role in the management of certain chronic painful conditions.[1] Tramadol 1.5 mg/kg IM did not lead to apnea.[32]

## Non-steroidal Anti-inflammatory Drugs

The NSAIDs provide analgesia and reduce inflammation. NSAIDs inhibit cyclo-oxygenase or lipoxygenase enzymes, which convert arachidonic acid, a fatty acid found in cell membranes that are released on damage, into prostanoids, which in turn generates inflammation and immune responses. NSAIDs are often dosed beyond their plasma half-life due to protein binding and high lipophilicity, which results in longer tissue concentrations. Assessment of drug efficacy has been evaluated through in vitro assays that measure cyclo-oxygenase inhibition and in vivo assays in several species that systematically assess pain control after an antinociceptive event.[1] Adverse systemic effects include gastrointestinal injury (less commonly reported in NHPs) and renal injury in compromised patients.

NSAIDs alone are insufficient to provide adequate analgesia after major surgery. By combining NSAIDs with drugs from other classes, most frequently opioids, reliable and effective analgesia with minimal side effects can be achieved. This combination is used frequently in laboratory animal medicine and should be considered the standard for surgical procedures that are expected to cause moderate to severe pain.[59]

Commonly utilized drugs in marmosets include meloxicam, carprofen, and ketoprofen. There is no evidence-based or pharmacokinetic studies using NSAIDs in marmosets or New World species. Given the high reliance on NSAIDs for analgesia management, studies to refine dosing in marmosets are needed. Suggested published doses include carprofen 4 mg/kg SC[16] and meloxicam 0.1–0.2 mg/kg SC PO q24 hours.[27] A sustained release formulation of meloxicam that provides up to 72 hours of analgesia based on plasma evaluations in cynomolgus macaques has been used in Old World species.[60] Several institutions have utilized the published macaque dose.[27] Adverse gastrointestinal side effects, although not described in marmosets, may occur as in other species when administered for longer periods.

## Local Anesthetics

Local anesthetics have the potential to completely block nociceptive signals from reaching the central nervous system through blocking ion channels, mainly voltage gated sodium channels.[1] Tissue infiltration prior to making a surgical incision is commonly utilized. Lidocaine has a quick onset and lasts for approximately 1 hour while bupivacaine has a slower onset (20 minutes) and lasts for approximately 3–10 hours.[1] A dose of bupivacaine 0.1 mL per site has been reported.[37] It is recommended not to exceed 2 mg/kg bupivacaine or 4 mg/kg lidocaine for infiltration blocks as neurotoxicity or myotoxicity may occur locally. Local anesthetics may be diluted to achieve appropriate volumes for adequate administration; prevention of nerve signal conduction requires contact with 3 or more nodes of Ranvier.[61] Central nervous system and cardiovascular toxicity may occur if systemic absorption exceeds recommended doses.[1] One author (Fitz) has used bupivacaine liposomal injectable suspension during surgical procedures in marmosets. Topical creams are also available for use prior to minor procedures such as catheter or tattoo placement.

## Adjunct Drugs

Gastrointestinal side effects, such as nausea and ileus, are associated with anesthetic administration and fasting. Symptomatic treatment will aid in return to normal function. Anti-nausea treatments include maropitant (1 mg/kg SC q24 hours), a neurokinin receptor antagonist, and ondansetron (0.2 mg/kg IM q24 hours), a serotonin receptor antagonist.[1] Acid secretion by parietal cells of the stomach is reduced through blocking of receptors. Famotidine (0.5–1 mg/kg IM IV PO q24 hours) is a histamine type 2 receptor antagonist. Omeprazole (0.5–1 mg/kg PO q24 hours) is a proton pump inhibitor. Both can be used perioperatively or when gastrointestinal ulceration is suspected.[1] Sucralfate (100–200 mg/kg PO q12–24 hours) aids in treatment of stomach and duodenal ulcers through coating the lesion and bismuth subsalicylate (5.25–10.5 mg PO q12–24 hours) can also reduce inflammation of the gastrointestinal mucosa and is antisecretory.

## Ancillary Treatments

Additional therapies utilized in marmosets include low-level laser therapy. One institution utilizes laser therapy for both incisional and traumatic wounds. The treatment can be applied while hand restrained and serves to promote wound healing and reduce inflammation, both of which reduce pain.[27]

## Analgesia Efficacy Monitoring

Individual variation in perception of pain and need for analgesia varies. Assessment of individuals with a species-specific system will ensure individuals receive adequate analgesia[53,62] (Fitz et al[49]). Ultrasonic vocalizations were evaluated as an indicator of stress in marmosets but were found unreliable.[48] Buprenorphine influences behavior in marmosets, and this may make pain assessment difficult.[53]

## ANESTHESIA AND ANALGESIA SUPPORT OF COMMON SURGICAL PROCEDURES IN MARMOSETS

All marmosets undergoing a surgical procedure should receive a thorough physical exam with care taken to assess hydration through evaluation of skin turgor, hematocrit, or electrolytes. Abnormal findings should be corrected to stabilize the animal prior to surgery. Anesthesia drug regimens must support the research or clinical objectives while maintaining balanced surgical anesthesia.

Marmosets are used for neuroscience applications, including cranial implants, craniotomies for injections or electrode placement, and evaluation of the somatosensory pathway. It has been demonstrated that stimulus-evoked response and functional connectivity are altered by propofol and fentanyl anesthesia in marmosets undergoing fMRI.[35] The response of the auditory cortical neurons to sound is also influenced by anesthetics. Sufentanil, an opioid, has facilitated neural recordings of auditory responses that were found to be impaired under isoflurane anesthesia.[36] For neurosurgical procedures, marmosets are generally secured in a stereotaxic device, and consideration of IV access and endotracheal tube security is critical. Research and veterinary staff must communicate clearly how this will be established and constantly observe the marmoset throughout the procedure. Inhalant anesthetics are usually preferred for longer procedures, but consideration of PIVA options may facilitate reduction of adverse effects commonly observed with inhalant anesthetics (increased intracranial pressure, decreased cardiac output and blood pressure, respiratory rate depression). Monitoring equipment access may be limited while the marmoset is secured in a stereotaxic device. Equipment should be tested prior to use to ensure it will not need to be manipulated frequently. Thermal support devices must be evaluated prior to surgery to ensure they will provide heat without disrupting stereotaxic use. Recovery from surgery and anesthesia will be enhanced if marmosets are well hydrated and thermally supported throughout the procedure. Thermal and nutritional support are required post surgery. Plan to have a quiet environment where marmosets can recover, and consider potential stress to marmosets in neighboring enclosures if placing marmosets requiring frequent care in densely populated animal rooms.

Reproductive manipulations commonly conducted in marmosets include caesarean section, oocyte collection, ovariectomy, and vasectomy.[6] Planned procedures allow careful presurgical evaluations as described above. Caesarean sections for clinical indications such as dystocia may present as an emergency and require immediate anesthetic induction. It then becomes critical to evaluate the dam immediately on removal of the fetuses to ensure adequate hydration and analgesia. Quick return to normal function will allow the dam to care for the newborn infants. Anesthetic selection should focus on maintaining adequate cardiac output to ensure blood supply to the fetuses. Propofol PIVA should be considered. Body positioning should elevate the hips to one side to reduce pressure on the large vessels underneath the uterus. Infant weights and activity level will guide decisions on whether supplemental nutrition is provided.[63,64]

## CONCLUSIONS

Adaptations to accommodate the unique physiology of the marmoset must be made to provide adequate anesthesia and analgesia. Institutions are refining various regimens, and through communication our collective knowledge can elevate our clinical practices.

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