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CLINICAL REVIEW

FELINE PROCEDURAL SEDATION AND ANALGESIA
When, why and how

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Practical relevance: Procedural sedation and analgesia (PSA) describes the process of depressing a patient's conscious state to perform unpleasant, minimally invasive procedures, and is part of the daily routine in feline medicine. Maintaining cardiopulmonary stability is critical while peforming PSA.

Clinical challenges: Decision-making with respect to drug choice and dosage regimen, taking into consideration the cat's health status, behavior, any concomitant diseases and the need for analgesia, represents an everyday challenge in feline practice. While PSA is commonly perceived to be an uneventful procedure, complications may arise, especially when cats that were meant to be sedated are actually anesthetized.

Aims: This clinical article reviews key aspects of PSA in cats while exploring the literature and discussing complications and risk factors. Recommendations are given for patient assessment and preparation, clinical monitoring and fasting protocols, and there is discussion of how PSA protocols may change blood results and diagnostic tests. An overview of, and rationale for, building a PSA protocol, and the advantages and disadvantages of different classes of sedatives and anesthetics, is presented in a clinical context. Finally, injectable drug protocols are reported, supported by an evidence-based approach and clinical experience.

Keywords: Acepromazine; agonists of α_2-receptors; alfaxalone; benzodiazepines; chemical restraint; ketamine; sedation

Sedation in cats: a routine challenge in feline practice

Sedation, chemical restraint and analgesia are part of the daily routine in feline practice. In some cats, especially those with fractious temperaments or showing fearful or excited behavior, sedation is required to render the patient cooperative. It is also used to facilitate diagnostics (eg, venipuncture for hematology, imaging, etc) (see box).

Examples of non-invasive procedures that may require procedural sedation and analgesia in cats

- Diagnostic imaging (radiography, ultrasound, echocardiography, CT)
- Physical and rectal examination (non-compliant or feral patients)
- Skin allergy testing and biopsy
- Urinary catheterization
- Minor laceration repairs
- Bandage changes
- Vascular access and/or venipuncture (eg, hematology, blood donation)
- Nasoesophageal feeding tube placement
- Abdomino-, cysto- or thoracocentesis
- Ophthalmic, otoscopic and oral examinations
- Nail trimming (some cats)

The ultimate goal of sedation is to provide comfort and often analgesia while reducing fear, anxiety and stress in these patients. Sedation will also prevent inadvertent injuries to personnel and promote a better hospital experience for cats undergoing minor procedures. However, the choice of drugs and dosage regimens can be challenging since there is no 'one size fits all'; protocols should be adjusted and adapted on a case-by-case basis. The clinician must consider the cat's health status and behavior, concomitant diseases, the need for analgesia, and the magnitude of the procedure and hence the level and duration of sedation required. Other challenges in sedation and analgesia include drug unavailability and lack of familiarity with specific medicines.

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Procedural sedation and analgesia (PSA) is a term used in human medicine to describe the process of depressing a patient's conscious state, in order to perform unpleasant, minimally invasive or objectionable procedures.[1] This clinical review explores the scientific literature to address complications and risk factors, as well as drug protocols used for PSA in cats. Recommendations are made using an evidence-based approach and the authors' experience.

It's not 'just a quick sedation': complications and risk factors

Sedation is regularly seen as an uneventful procedure with a low risk of complications. However, some protocols used for PSA may induce unconsciousness, amnesia and the loss of protective reflexes (ie, general anesthesia). There may be a mistaken belief that these patients are 'just sedated' when they are, in fact, anesthetized, and a more comprehensive monitoring and supportive care plan should be in place given that complications may easily arise. In addition, PSA is not always safer than general anesthesia and is often chosen for its practicality rather than representing the best option for the cat. For instance, general anesthesia offers better airway control and an easy means of ventilation, monitoring and oxygenation when cats are intubated for more extensive and invasive procedures. A study showed that profound sedation may not be suitable for all patients and can increase the risk of anesthesia-related death.[2] Therefore, the decision between PSA and general anesthesia should be taken cautiously, evaluating the advantages and disadvantages of each technique.

Documented risk factors for sedation-related morbidity and mortality are scarce in the veterinary literature.[2–4] When risks have been reported, they are often presented in combination with data from anesthetized patients.[2,3] This creates difficulty in distinguishing sedation- from anesthesia-specific risk factors. However, one study reported that the risks of mortality following sedation and anesthesia are not significantly different.[3] Extrapolation from previous studies evaluating sedation- and anesthesia-related risk factors can, therefore, provide useful information when determining the likelihood of complications during PSA.

Cats have a higher risk of anesthetic death than dogs.[2,3,5–7] The rate of mortality following anesthesia and/or sedation in cats can be as high as 0.24%.[3] The primary causes for anesthesia- or sedation-related mortality in cats are presented in Figure 1. An association between extremes in age and body weight and an increased risk of mortality following sedation and anesthesia has been recognised in cats.[2,3] Senior and pediatric patients are more susceptible to the depressant effects of anesthetics, have prolonged recovery due to decreased hepatic blood flow and impaired thermoregulation, and have limited ability to respond to abnormal physiologic states such as hypotension.[3,8] Obese patients are not only susceptible to comorbidities due to an enhanced pro-inflammatory state, but they also have reduced cardiovascular reserves and impaired ventilation and mobility due to excessive fat deposition.[3] Intravenous (IV) access, endotracheal intubation and cardiopulmonary monitoring can be difficult in small cats and kittens. In terms of cat breeds, Himalayans have an increased risk of complications, likely due to their brachycephalic conformation,[9] making them prone to respiratory compromise and aspiration pneumonia during anesthesia.[10,11] Other risk

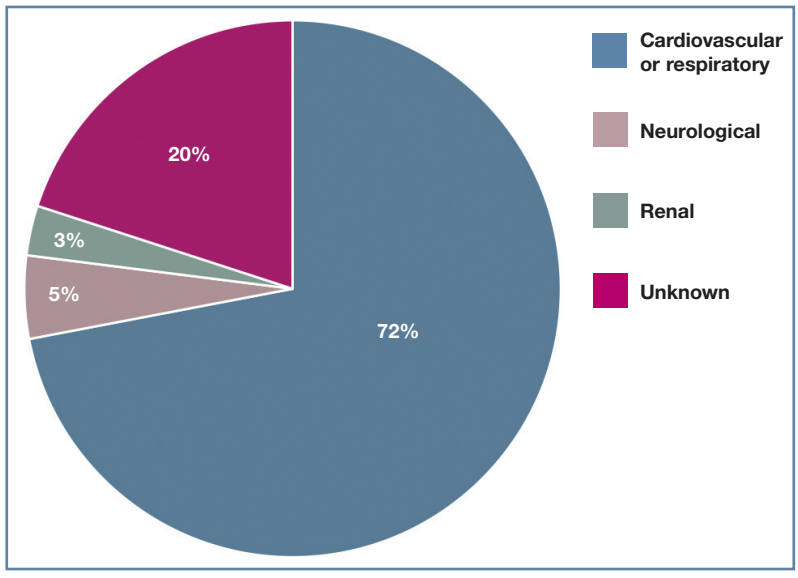

Figure 1 **Primary causes of sedation- and anesthesia-related deaths in cats.** *From Brodbelt et al (2008)*[5]

Some protocols used for PSA may induce unconsciousness, amnesia and loss of protective reflexes.

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Table 1 Factors increasing mortality in cats undergoing procedural sedation and anesthesia[2,3,6]

	Risk factors	OR*
ASA PS	ASA PS ⩾III vs ⩽II	3.0–4.0
	ASA PS I and II increasing to III	4.0
	ASA PS III increasing to IV	3.0–3.7
	ASA PS IV increasing to V	3.0
	ASA PS V vs III	13.4
Procedure	Non-elective vs elective	5.0–6.0
	Procedural urgency	1.6
	Change in urgency status (elective to urgent or urgent to emergent)	1.6
	Major vs minor procedure	3.0
Anesthetic protocol	Premedication + thiopental + isoflurane vs 'other' anesthesia protocols†	10.0
	Endotracheal intubation for minor procedures	2.0
	Excessive fluid therapy	4.0
	Lack of pulse oximetry monitoring	5.0
Patient demographics	>12 years vs 0.5–5 years	2.0
	<2 kg vs 2–6 kg	16.0
	>6 kg vs 2–6 kg	3.0
	Himalayan breed	4.0

ASA PS = American Society of Anesthesiologists physical status
*Odds ratio (OR) in this context is the odds that death will occur given a particular condition or circumstance. An OR >1 indicates increased occurrence of mortality
†'Other' included induction agents other than thiopental, propofol or ketamine alone and maintenance with agents other than isoflurane. For example, use of fentanyl, isoflurane, benzodiazepines or etomidate, or ketamine or thiopental with a coinduction agent

factors for feline sedation- and anesthetic-related death are detailed in Table 1.

Fluid therapy may be required during PSA. The administration of inappropriate quantities of IV fluids has been found to significantly increase the likelihood of anesthesia- and/or sedation-related deaths in cats.[3] Guidelines for maintenance fluids rate during anesthesia have been published in cats, recommending a significantly lower rate than previously suggested (3–5 vs 5–10 ml/kg/h).[12] Inappropriate use of IV fluids in euvolemic patients can result in volume overload and the development of pulmonary and peripheral edema. A thorough evaluation of the patient's hydration status and estimated losses during the procedure should help guide the veterinarian in determining if IV fluids are required, and the type and rate of administration to compensate for any ongoing losses and dehydration.

Lastly, fasting may reduce the risk of regurgitation and aspiration pneumonia and, in turn, the sequelae of desaturation, hypoxemia, sympathetic activation and potentially death (see 'patient assessment and preparation before PSA'). Veterinarians should thus avoid or minimize regurgitation and consider general anesthesia with intubation of the trachea in cats with severe central nervous system, respiratory, cardiovascular or gastrointestinal disorders.

Pre-examination and assessment sedatives: gabapentin and trazodone

Cats often show signs of fear and aggression when presenting at a veterinary clinic, which can pose problems during the intitial assessment. At-home oral sedatives that pet owners can administer may – in conjunction with feline-friendly handling – alleviate stress and anxiety in these patients, providing a safer environment for staff and a more pleasant experience for the animal (see box below).

Gabapentin is an antiepileptic, non-controlled medication, available in capsule or liquid form for oral administration. The administration of 100–150 mg oral gabapentin by the pet owner 90 mins prior to placing the cat in its carrier for transportation to a veterinary hospital can reduce stress and anxiety. It may also increase compliance in cats associated with the veterinary examination.[13] Owners typically report that their cats experience mild to marked sedation, display increased affectionate behavior and also reduced fear of dogs.[13] Peak clinical effects occur 2–3 h after administration and resolve within 8 h.[13] Adverse effects associated with this technique are rare, but may include vomiting, hypersalivation, minor muscle fasciculations and anisocoria.[13,14] Vomiting may be specific to the 100 mg capsules,[13] as the authors have not witnessed this side effect with the oral liquid formulation. It is not clear if gabapentin provides clinical analgesia in cats;[15] therefore, an opioid should be considered in painful patients or for minimally invasive procedures. Lower doses (50 mg orally) may reduce fear without resulting in measurable sedation for over 3 h post-administration.[14]

Trazodone, a serotonin antagonist and reuptake inhibitor, may reduce stress and fear in cats.[16] Oral administration of 50–100 mg provides sedation, reduces anxiety during transport, reduces activity and improves ease of handling during veterinary examination.[16,17] Recommendations are to administer trazodone 60–90 mins prior to transport or 90–120 mins prior to veterinary examination.[16] Peak effect is approximately 2–3 h following oral administration.[17]

Gabapentin and trazodone have minimal effects on the cardiopulmonary system,[13,16] and therefore may be excellent sedatives in systemically ill non-compliant cats.

Oral sedation for transport and hospital examination

- Dosing recommendations:
  - Gabapentin: administer 100–150 mg 90 mins prior to patient transport to the veterinary clinic.
  - Trazodone: administer 50–100 mg 60–90 mins prior to patient transport to the veterinary clinic.
- Peak onset of effect: 2–3 h following administration.
- Duration of effect: dose-dependent, up to 8 h following administration.
- Reduces fear and anxiety during hospital visitation and pre-sedation examination.
- Minimal effects on the cardiopulmonary system.
- If moderate sedation is observed following trazodone or gabapentin administration and further PSA drugs are required, consider reducing the PSA drug doses by 25–50%.

Patient assessment and preparation before PSA

Preanesthetic assessment should be performed in cats before PSA as it may identify potential risk factors and avoid complications. It is not uncommon for a procedure to start under PSA and evolve into a more complex anesthetic challenge. There is a particular problem when procedures become significantly more painful and inadequate analgesia (eg, a weak opioid analgesic) has been administered as part of the PSA protocol. In these circumstances, alternative analgesic agents may be required as the weaker opioids (eg, butorphanol or buprenorphine) may negatively impact the analgesic efficacy of pure opioid agonists (eg, morphine, methadone and hydromorphone).[18,19]

The patient's identification should be confirmed and its medical history reviewed, focussing on previous procedures, and any concomitant medications and diseases. This is also the time to discuss with clients the risks associated with PSA and the planned procedure. Some cats may need fluid therapy and stabilization before PSA; fasting protocols should be in place. Current recommendations include shorter fasting times (3–4 h) when compared with dogs.[20] The administration of a small amount of wet food 3–4 h before sedation may reduce gastroesophageal reflux and acidic reflux.[20] Water should be available until the time of PSA. Specific developmental stages (neonatal, pediatric) and conditions such as gastrointestinal and central nervous system disease or diabetes, brachycephalic conformation or a history of gastroesophageal reflux and/or aspiration may require specific fasting times based on the patient's individual needs, and further information can be found elsewhere.[21]

The assignment of American Society of Anesthesiologists (ASA) physical status is important to predict complications and identify the risk of anesthetic-related death (Table 1).[2,3] Feline-friendly handling techniques should always be adopted (gentle approach, patience, positive attitude, appropriate petting, etc) (Figure 2). Cats with a timid or fearful demeanor should be examined in their carriers; top- or side-opening carriers provide a safe and secure environment for these individuals (Figure 3). Indeed, the cat's behavior is important in the decision-making process involving PSA and dosage regimens. Blood collection for additional laboratory diagnostics (ie, hematology and blood chemistry analysis), if needed, can be performed after drug administration and during venous catheterization. The authors will often use the blood extracted from the catheter hub to perform a hematocrit and total protein evaluation and avoid unnecessary jugular venipuncture. However, venous catheterization may not always be performed as part of the PSA protocol and there is no consensus on the administration of fluid therapy in these cats. Additionally, hematocrit values in some cases may decrease by up to 30% after the administration of sedatives, especially dexmedetomidine, ketamine and acepromazine.[22,23] (Clinicians should also be aware of the potential for increased ultrasonographic and radiographic splenic measures after the administration of acepromazine;[22] and several drugs used during PSA may change echocardiographic results, as discussed later.)

Figure 2 Feline-friendly handling techniques should be used throughout procedural sedation and analgesia (PSA) to minimize stress and fear and provide a good hospital experience. The mantras 'less is more' and 'go slow to go fast' are true during feline handling. Towels can be used around the neck and body for physical restraint and gentle care, and to avoid scruffing. An Elizabethan collar will provide additional protection for the handler from aggressive cats. This particular patient is safely restrained for a procedure such as intramuscular injection or intravenous catheter placement

The authors often use the blood extracted from the venous catheter hub to perform a hematocrit and total protein evaluation and avoid unnecessary jugular venipuncture.

Figure 3 Cats may be examined and handled in top-opening or side-opening carriers to facilitate the procedure and maximize comfort during veterinary consultations

It is good practice to have an anesthetic machine and means of intubation and ventilation available when sedation is profound, with a risk of regurgitation and aspiration, and/or with patients that are at high risk of complications.

Materials, supplies and equipment should be ready and in good order before PSA. Prevention is key to avoiding complications. Doses and volumes of emergency drugs should be calculated beforehand. It is good practice to have an anesthetic machine and means of intubation and ventilation available when sedation is profound, with a risk of regurgitation and aspiration, and/or with patients that are at high risk of complications (ie, senior or pediatric patients, or those with extremes of body weight) (Figure 4).[2–4] In some practices, an anesthetic machine may not be available. Oxygenation may still be required, and portable oxygen cylinders should be available. Oxygen supplementation may be needed to prevent or treat hypoxemia in cats undergoing PSA.[24] A manual resuscitation bag is a practical means of providing oxygenation (Figure 4).

Hypothermia can be avoided by using a warming system (ie, forced air warming blanket or circulating warm water device) to prevent heat losses during PSA. Additional measures for the prevention of hypothermia include use of bubble wrap, blankets and quilts, or the Hibler's method. The last is a low-cost technique combining an outer vapor barrier (ie, plastic wrapping) with an inner insulating layer (ie, blankets).[25] In humans, the Hibler's method has been shown to reduce hypothermia and promote faster rewarming than use of blankets and bubble wrap.[25]

Figure 4 Supplies prepared in advance of PSA, in case intubation of the cat's trachea is required. a = cuffed endotracheal tube; b = cuff inflation syringe; c = lidocaine with a syringe and catheter for topical application on the arytenoids to prevent laryngospasm during intubation; d = topical eye lubrication; e = sterile endotracheal tube lubrication; f = roll gauze for securing the endotracheal tube in place; g = mask for oxygen supplementation; h = square gauze to help grasp the patient's tongue during intubation; i = laryngoscope; j = stylet for placement within the endotracheal tube; the stylet should be introduced only as far as 3–5 cm past the arytenoids, and is removed once the endotracheal tube is in place, taking care not to cause pharyngeal or tracheal trauma; k = manual resuscitation bag and attachment for oxygen insufflation. Note: A Mapleson D (Bain) non-rebreathing circuit attached to an anesthetic machine may be used in lieu of a manual resuscitation bag at flow rates of 150–300 ml/kg/min

Drug protocols for PSA: overview and rationale

Before focussing on specific injectable protocols for PSA, some important principles deserve particular mention. Firstly, patient assessment incorporating health status and behavior is paramount when choosing a drug protocol for PSA. So too is an individualized approach, allowing adjustments to doses and protocols as required. The ideal protocol should maintain appropriate cardiorespiratory function while unpleasant, minimally invasive procedures are performed. What constitutes 'appropriate' for each cat undergoing PSA is vague. For example, a healthy cat may tolerate decreases in cardiac output and heart rate induced by agonists of alpha(α)$_2$-adrenergic receptors during hip radiography. Similar changes in cardiovascular function could, however, be severely detrimental in a senior cat with sepsis and undergoing abdominal ultrasonography.

When possible, neuroleptanalgesia is recommended during PSA and involves the combination of an opioid analgesic and a tranquillizer (ie, acepromazine) or sedative (benzodiazepine).[26] This has the potential benefits of producing a greater degree of sedation and analgesia with reduced adverse cardiopulmonary effects when compared with either drug administered alone at similar doses. Clinical judgment is important in the decision-making process and antagonist agents (ie, atipamezole, flumazenil or naloxone) should always be available and drawn-up ready for use in critical cases. Butorphanol has been reported to preserve analgesia better than naloxone when used as a reversal agent in cats.[19]

The ideal protocol should maintain appropriate cardiorespiratory function while unpleasant, minimally invasive procedures are performed.

Neuroleptanalgesia produces a greater degree of sedation and analgesia, with reduced cardiopulmonary events, compared with use of the component drugs (opioid analgesic plus tranquillizer or sedative) administered alone at similar doses.

Acepromazine, benzodiazepines (ie, diazepam or midazolam) or agonists of α_2-adrenergic receptors (ie, dexmedetomidine, medetomidine or xylazine) are used in combination with an opioid for PSA (Table 2). Local anesthetic blocks are not specifically discussed in this article, but should be incorporated to provide a smooth PSA while decreasing drug requirements.

Note that alternative methods for achieving PSA, such as chamber induction using inhalant anesthetics, can be useful to protect handlers from injury but may cause airway irritation[28] and an excitatory phase in patients,[29] in addition to the environmental concerns over waste anesthetic gases.[30] Moreover, this technique may be associated with increased risk of anesthetic-related morbidity or mortality due to the excessive inhalant anesthetic concentrations required to induce adequate sedation and avoid involuntary excitement.[20]

Table 2 Examples of neuroleptanalgesia protocols used for procedural sedation and analgesia (PSA) in cats.[27] If necessary, these suggested protocols can be used for premedication prior to induction of general anesthesia

Drug combination	Dose (mg/kg) and route*	Comments
Dexmedetomidine combinations for cats ASA PS I–II		Caution in critically ill patients and those with bradyarrhythmias. Low doses may be beneficial in patients with left ventricular outflow obstruction and HCM. Useful in procedures when heavy sedation is required
Dexmedetomidine + butorphanol	0.01 + 0.2 IM	Provides good sedation for non-invasive diagnostic procedures (radiography, ultrasound examination, and thoraco-, cysto- and abdominocentesis), phlebotomy, intravenous catheter placement, minor procedures or procedures that result in mild pain in healthy cats. Provides minimal analgesia
Dexmedetomidine + buprenorphine†	0.01 + 0.02 IM	Provides good sedation and mild to moderate analgesia for the above procedures
Dexmedetomidine + hydromorphone *or* methadone‡	0.01 + 0.1 *or* 0.5 IM	Provides excellent sedation and analgesia for the above procedures and for procedures that result in moderate to severe pain
Dexmedetomidine + hydromorphone *or* methadone + ketamine	0.01 + 0.1 *or* 0.5 + 3 IM	May produce profound sedation. Provides excellent analgesia for the above procedures and for procedures that result in moderate to severe pain. May produce some dysphoria during emergence from sedation. Ketamine may elicit pain on injection. Caution when using ketamine in cats with HCM due to its sympathomimetic effects on heart rate
Acepromazine combinations for cats ASA PS I–II		Caution in hypovolemic, critically ill or hypotensive patients. Better suited to more protracted procedures due to its long duration of action and lack of reversibility
Acepromazine + butorphanol	0.05 + 0.2 IM	Mild sedation for non-invasive diagnostic procedures (radiography, ultrasound examination), phlebotomy, intravenous catheter placement
Acepromazine + buprenorphine†	0.03 + 0.02 IM	Good analgesia for procedures that result in mild to moderate pain. Euphoria rather than sedation may be present
Acepromazine + hydromorphone *or* methadone‡	0.03 + 0.1 *or* 0.5 IM	Mild sedation as described for the other acepromazine combinations. Good analgesia for procedures that result in moderate to severe pain
Other combinations		
Midazolam + butorphanol + ketamine	0.3 + 0.3 + 5 IM	Effective chemical restraint for fractious cats ASA PS III or IV. Minimal effects on the cardiovascular system. Does not always produce profound sedation and vocalization may be present; however, patients are often compliant for most minor procedures. Ketamine may elicit pain on injection. Caution when using ketamine in cats with HCM due to its sympathomimetic effects on heart rate. Alfaxalone (2–3 mg/kg) can replace ketamine. Oxygen supplementation and endotracheal intubation equipment should be available when using injectable anesthetics
Methadone *or* hydromorphone‡ + midazolam	0.5 *or* 0.1 + 0.25 IM	Provides adequate sedation in pediatric (<12 weeks), senior (>75% normal life expectancy for the breed) or ASA PS ⩾IV patients. μ-opioid receptor agonists can be replaced with butorphanol or buprenorphine for non-painful or mildly painful procedures, respectively

*If additional doses of PSA drugs are required due to decreases in depth of sedation, the authors recommend administering 25–50% of the original dose
†Buprenorphine at standard concentration (0.3 mg/ml)
‡Other full μ-opioid receptor agonists can be used (ie, fentanyl, oxymorphone, morphine)
ASA PS = American Society of Anesthesiologists physical status; HCM = hypertrophic cardiomyopathy; IM = intramuscularly

The magnitude/level of sedation and analgesia and the quality of recovery are better with the combination than with each drug used alone;[31,32] lower doses of each drug can normally be administered. Also, adverse effects may be reduced with neuroleptanalgesia. For example, in a prospective, randomized, blinded study of 30 cats, the prevalence of vomiting was 70% when dexmedetomidine was used alone, compared with 10% after dexmedetomidine–butorphanol.[33] The dose of single-agent dexmedetomidine also had to be increased two-fold to produce similar sedative effects to a combination of dexmedetomidine with butorphanol or meperidine (pethidine) for various clinical procedures.[33] However, there are some occasional cases where opioids are used alone for PSA or when the specific combination of benzodiazepine–opioid is indicated (see box on right). The specific choice of opioid will depend on the onset, duration and level of analgesia required for the procedure (see box on left; Table 3). For further information, readers are referred elsewhere.[18,34–36]

Factors to consider when choosing an opioid analgesic in cats

- Severity of pain
- Duration of action
- Onset of action
- Route of administration (ie, IM vs SC vs IV vs buccal)
- Level of sedation desired
- Avoidance of unwanted adverse effects (ie, nausea, vomiting, histamine release, bradycardia)

Sedation is superior when agonists of α_2-adrenoreceptors are administered alone or in combination with opioids when compared with acepromazine alone or with an opioid, and also benzodiazepine-based protocols.[22,23] Ketamine, tiletamine–zolazepam and alfaxalone-based protocols have also been used for neuroleptanalgesia to provide robust chemical restraint (Table 4). However, sedative effects may vary according to dosage regimens, individual patient variability in response to the drugs, disease and patient behavior, and the quality of sedation is sometimes unpredictable.

Opioids or opioid–benzodiazepine combinations may provide useful sedation in cats in some specific cases

- Extremes of age (⩽12 weeks or ⩾75% of breed's predicted life expectancy)
- ASA PS ⩾IV (ie, lower urinary tract disease, polytrauma, hypovolemia, sepsis)
- Central nervous system pathology (ie, space-occupying lesions, head trauma)
- Moderate to severe cardiovascular disease (ie, hypertrophic cardiomyopathy [HCM])
- Severe multiorgan dysfunction (ie, hepatic, renal, endocrine)

The following section provides additional information on protocols commonly used for PSA in cats using an evidence-based approach. Detailed pharmacology of these drugs is not presented herein. Drug combinations for PSA are also routinely used for premedication, with important anesthetic-sparing effects.

Table 3 Opioids commonly used for procedural sedation and analgesia in cats[34]

Opioid	Dose (mg/kg)	Frequency of administration	Route of administration	Comments
Pure μ-opioid receptor agonists				For moderate to severe pain relief
Methadone	0.3–0.5	q4–6h	IM, IV, OTM	Has NMDA receptor antagonist properties
Hydromorphone	0.05–0.1	q4–6h	IM, IV	Hyperthermia may be observed. Vomiting observed with IM route
Morphine	0.2–0.4	q4–6h	IM, IV	Slow administration is recommended with IV route due to potential for histamine release. Histamine release is dose-dependent. Vomiting may be observed with IM route
Oxymorphone	0.025–0.1	q4–6h	IM, IV	–
Fentanyl	0.002–0.01	q20–30 mins	IV	May produce more pronounced cardiopulmonary depression than other opioids. Consider as a CRI (2–15 μg/kg/h) for procedures longer than 30 mins
Meperidine (pethidine)	3–5	q1–2h	IM	Do not administer IV due to histamine release. May produce increases in heart rate
Partial μ-opioid receptor agonists				Provide mild to moderate pain relief
Buprenorphine 0.3 mg/ml	0.02–0.04	q4–8h	IM, IV, OTM	May produce euphoria
Buprenorphine 1.8 mg/ml	0.24	q24h up to q3 days	SC, OTM	For the treatment of postoperative pain. Not recommended for short procedural sedations
Weak μ-opioid receptor agonist or μ-opioid receptor antagonist/ κ-opioid receptor agonist				Provides minimal pain relief
Butorphanol	0.2–0.4	q1–2h	IM, IV	Consider for diagnostic procedures only. May provide enhanced sedation when compared with other opioid classes

IM = intramuscular; IV = intravenous; OTM = oral transmucosal (buccal); NMDA = N-methyl D-aspartate; CRI = constant rate infusion; SC = subcutaneous

Drug protocols for feline PSA: an evidence-based approach

The sedative, cardiorespiratory and metabolic effects of, as well as quality of recovery for, several drug combinations for feline PSA have been reported (see Table 4 for an overview). These drug combinations, together with some additional PSA protocols, are discussed in the text below.

It is important to bear in mind that comparisons are difficult between these studies. A scoring system for feline sedation assessment has not been validated. Most studies have evaluated sedation using interactive visual analog and simple descriptive scales that are

Drug combinations for PSA are also routinely used for premedication, with important anesthetic-sparing effects.

Table 4 Selected drug protocols used in published studies for procedural sedation and analgesia (PSA) in cats (continues on page 1037)

Drug combination	Doses, route of administration, procedure/endpoint	Comments	Reference(s)
Tiletamine–zolazepam + methadone (TZM)	3 mg/kg + 0.2 mg/kg IM; before neutering	❖ Better restraint for venous catheterization and higher sedation scores than acepromazine (0.03 mg/kg) and methadone (0.2 mg/kg) (AM) IM but similar HR and RR 25 mins after injection ❖ Similar anesthetic-sparing effect during neutering and time to extubation and sternal recumbency to AM. Time to standing longer with TZM	37
Tiletamine–zolazepam (TZ)	5 mg/kg or 7.5 mg/kg buccally; no endpoint	❖ 0.1 ml/kg or 0.15 ml/kg, respectively, of the combination is administered into the cheek pouch. Onset and duration of action are approximately 15 mins and 120 mins, respectively ❖ Sedative effects were not significantly different and there seems to be no benefit in using high vs low doses of TZ alone buccally, especially considering that systolic BP and RR were lower in high- vs low-dose TZ ❖ Hypersalivation was observed in 3/7 cats with the high dose of TZ ❖ Dysphoria was observed in the recovery phase but not thoroughly reported	38
Tiletamine–zolazepam + ketamine + xylazine (TKX)	500 mg TZ (1 vial) reconstituted with 4 ml ketamine (100 mg/ml) and 1 ml xylazine (100 mg/ml) IM; before neutering	❖ Cats were administered 0.25 ml of the TKX solution IM ❖ Monitor closely for hypoxia as SpO_2 fell below 90% in most cats ❖ Prolonged recoveries even when reversed with yohimbine (72 ± 42 mins from reversal to sternal recumbency) ❖ Patients may require additional analgesia for more painful procedures	39
Acepromazine + butorphanol ± ketamine (AB or ABK, respectively)	0.1 mg/kg + 0.25 mg/kg ± 1.5 mg/kg IM; echocardiography	❖ Sedation scores or quality of sedation were not recorded ❖ Increases in HR seen after ABK and decreases in BP after AB ❖ Changes in echocardiographic variables were not deemed clinically relevant, except for decreases in preload and increases in diastolic wall thickness that could be mistaken for hypertrophy (ie, pseudohypertrophy)	40
Alfaxalone ± dexmedetomidine (AD)	5 mg/kg ± 20 µg/kg IM; no endpoint	❖ High volume of administration may be an issue with IM injection ❖ Moderate to profound sedation with alfaxalone alone, suggesting robust chemical restraint with minor cardiorespiratory changes ❖ General anesthesia is achieved with AD in a dose-dependent manner. All cats could be intubated with the combination. Decreases in HR and increases in BP were observed with AD. Desaturation can be recorded with high-dose dexmedetomidine ❖ Some adverse effects may be observed in the recovery phase: alfaxalone can produce ataxia and dysphoria; vomiting, ataxia and hyperkinesia may be observed with the AD combination	41
Alfaxalone	Doses of 1, 2.5, 5 and 10 mg/kg (IM) or 5 mg/kg (IV); no endpoint *or* 2 or 5 mg/kg IM; diagnostic or non-invasive procedures	❖ Large volumes required for IM injections, especially in the 5 mg/kg and 10 mg/kg groups ❖ Time to lateral recumbency was less than 7 mins in all cats, except for the 1 mg/kg group. Dose-dependent duration of sedation was observed, with lateral recumbency for more than 1 h in the 5 mg/kg and 10 mg/kg groups ❖ Poor anesthetic recovery with ataxia, muscle tremors, paddling and opisthotonos precludes the use of alfaxalone as a single sedative agent in feline practice ❖ Inadequate sedation was recorded for both 2 mg/kg and 5 mg/kg alfaxalone in 10 cats and these animals were excluded from the trial	24, 42
Dexmedetomidine ± hydromorphone + alfaxalone (DHA or DA, respectively)	10 µg/kg ± 0.1 mg/kg + 5 mg/kg IM; endotracheal intubation	❖ Both protocols induced light depth of anesthesia according to bispectral index monitoring. Large volumes of alfaxalone are injected IM ❖ Time to loss of withdrawal reflex and intubation was shorter in cats receiving DH than D before alfaxalone. All cats were intubated when using both protocols. Spontaneous movement during light anesthesia ❖ Prolonged recovery, marked hyperactivity, excitement and ataxia were observed in both the DA and DHA groups. Quality of recovery was not improved with the addition of hydromorphone	43

dependent on the observer's experience, leading to large inter-study variability.[56] Various multidimensional scales for sedation scores have also been used but with little validation.[24,44,57] Different doses, drug combinations and routes of administration have been reported using either clinical or experimental populations. Protocols have been reported for a single procedure (ie, echocardiography) or for premedication, which cannot be generalized to other situations.

Table 4 Selected drug protocols used in published studies for procedural sedation and analgesia (PSA) in cats (continued from page 1036)

Drug combination	Doses, route of administration, procedure/endpoint	Comments	Reference(s)
Alfaxalone + butorphanol (AB)	2 mg/kg + 0.2 mg/kg IM; echocardiography or diagnostic/non-invasive procedures or venipuncture for blood collection *or* 5 mg/kg + 0.2 mg/kg IM; diagnostic/non-invasive procedures *or* 2–3 mg/kg + 0.4 mg/kg IM; venipuncture for blood collection *or* 2–3 mg/kg + 0.2 mg/kg SC; oral radioiodine administration	✣ Onset and duration of lateral recumbency were 5–10 mins and 35 mins approximately, respectively. Time to standing was around 45 mins. Good for outpatient procedures ✣ Median recumbency time was 53 mins after AB for blood collection ✣ AB produced chemical restraint with some mild systolic depression (decreased left ventricular fractional shortening and ejection fraction) ✣ AB produced similar sedation to dexmedetomidine (10 µg/kg) and butorphanol (0.2 mg/kg; DB) IM. Muscle relaxation was better with DB than AB ✣ Cats that did not achieve lateral recumbency with either DB or AB tolerated gentle physical restraint for blood collection ✣ Quality of recovery was similar for DB and AB ✣ High volumes of administration for alfaxalone required two injections. Two cats receiving 2 mg/kg of alfaxalone for AB did not become recumbent and several cats required additional sedation. High doses of alfaxalone (5 mg/kg) in AB produced superior sedation than 2 mg/kg in AB, but also prolonged recovery. Some cats required oxygen supplementation ✣ Peak sedation between 30 mins and 45 mins after SC administration of AB, but enough for the administration of radioiodine in hyperthyroid cats. Tremors and increased sensitivity to noise were observed	24, 44–47
Dexmedetomidine + butorphanol (DBUT) or buprenorphine (DBUP)	10 µg/kg + 0.4 mg/kg (DBUT) or 0.02 mg/kg (DBUP) IM; imaging, blood sampling, wound care and chemotherapy *or* 40 µg/kg + 0.01 mg/kg (DBUP) IM; echocardiography	✣ Higher sedation scores with DBUT than DBUP ✣ Maximal sedation achieved in 10 mins ✣ High prevalence of post-administration vomiting with DBUP ✣ Some cats required additional administration of alfaxalone (1.5 mg/kg IM) for venous catheterization ✣ DBUP produced chemical restraint (with no need for physical restraint) for echocardiography using high doses of dexmedetomidine (Johard et al 2018).[49] Ventricular and atrial diameters and BP increased; flow velocities, fractional shortening and HR decreased, which could confound diagnosis of cardiomyopathy ✣ Vomiting after oral and IM administration was observed in 4/6 and 3/6 cats, respectively. Hypersalivation may also be seen following oral administration, which could impair drug absorption	48,49
Ketamine + midazolam	14 mg/kg + 0.5 mg/kg intranasal or IM; no endpoint	✣ Similar levels of sedation when both routes of administration were compared ✣ In the intranasal group, cats reacted with snorting and/or sneezing. In the IM group, excessive vocalization and changes in behavior suggested pain at injection ✣ The nasal mucosa has great vascularization and high permeability that may contribute to rapid drug absorption ✣ The authors commonly use a lower dose of ketamine (ie, 5–10 mg/kg) when administered IM	50
Medetomidine alone ± buprenorphine	30 mg/kg of medetomidine alone, or 10, 30 or 50 µg/kg with 0.02 mg/kg of buprenorphine IM; premedication before ovariohysterectomy	✣ Medetomidine (30 µg/kg) + buprenorphine (0.02 mg/kg) produced a significant isoflurane-sparing effect when compared with medetomidine alone ✣ Different doses of medetomidine (10, 30 or 50 µg/kg) with buprenorphine provided better anesthetic recoveries when compared with medetomidine alone	32
Ketamine + dexmedetomidine (KD)	3 mg/kg + 5 µg/kg IM; echocardiography	✣ Similar sedation scores to midazolam (0.4 mg/kg) + butorphanol (0.4 mg/kg) with ketamine (3 mg/kg) (MBK) or dexmedetomidine (5 µg/kg) (MBD) IM ✣ KD produced significantly shorter times to sternal recumbency and standing than MBD, but not MBK. However, atipamezole was not administered to cats after MBD ✣ Quality of recovery was superior with KD compared with MBK ✣ Vomiting was observed in 4/6 cats with KD ✣ Significant changes in hemodynamic parameters were observed after KD and MBD (see text)	23
Xylazine *or* dexmedetomidine with ketamine (XK or DK, respectively)	1 mg/kg or 5 µg/kg with 3 mg/kg IM; short left eye electroretinography	✣ Yohimbine (0.5 mg/kg) or atipamezole (25 µg/kg) were administered IM for reversal 30 mins after XK or DK injection ✣ Similar onset of action between treatments but cats in the XK group required longer to elevate the head and achieve standing position ✣ The protocol was effective for short sedation used for electroretinography	51

Additional PSA protocols are described within the text
IM = intramuscular; HR = heart rate; RR = respiratory rate; BP = blood pressure; SpO_2 = saturation of peripheral oxygen; IV = intravenous; SC = subcutaneous
Note: Some PSA protocols may significantly impact diagnostic testing (eg, echocardiography and blood work analysis; Table 5) and this should be considered when interpreting the results

Table 5 Effects of procedural sedation and analgesia protocols on diagnostic tests

Diagnostic test	Drug combinations	Effects on diagnostic tests	Comments	Reference(s)
Hematology	Propofol–ketamine–dexmedetomidine	Decreased: – Red blood cells – Packed cell volume – Hemoglobin concentration – Mean cell volume – Plasma total protein	Due to pooling of circulating blood cells in the spleen or other vascular reservoirs owing to decreased sympathetic activity	23, 52, 53
	Acepromazine	Decreased: – Packed cell volume		53
Biochemistry	Ketamine–dexmedetomidine	Decreased: – Lactate concentrations Increased: – Plasma glucose concentrations	Xylazine and medetomidine result in dose-dependent increases in glucose via inhibition of insulin secretion by agonists of α_2-adrenoreceptors. Caution with the use of α_2-adrenoreceptor agonists in diabetic cats	3, 54
Echocardiography and radiography	Dexmedetomidine combinations	Increased: – Cardiac silhouette size – Vertebral heart score – End-diastolic volume – End-systolic volume Decreased: – Ejection fraction – Fractional shortening	Presumed to be due to increased systemic vascular resistance and afterload. Interpret with caution depending on drug protocol	23, 49, 55

Acepromazine combinations

Acepromazine blocks dopaminergic receptors and decreases reaction to external stimuli. The drug has been used in combination with butorphanol, buprenorphine or methadone as premedication in clinical trials.[58–61] Sedation was not always systematically evaluated. These combinations produce a mild calming effect with third eyelid protrusion, purring and kneading, or a state of tranquilization for 2–3 h.[58,60–62] Moderate sedation following acepromazine administration was also effective in lowering propofol dosing requirements for anesthetic induction in cats.[59]

In some studies, a eutectic mixture of lidocaine–prilocaine cream was applied over the cephalic vein, and protected with occlusive dressing, after premedication with acepromazine–buprenorphine and approximately 20–30 mins before IV catheterization. This technique avoids excessive physical restraint and behavioral responses to manipulation, especially in cats responding poorly to the sedation.[18,60,61] Indeed, the application of this local anesthetic cream reduced the reaction of cats to IV catheterization, as assessed by a numerical rating scale.[63] Even so, acepromazine–opioid combinations will usually produce mild sedation and experienced support staff or veterinarians are often needed for physical restraint and handling.[64]

Acepromazine should not be used for PSA in cats with hypovolemia or dehydration, or in procedures with high risk of bleeding (Table 2). Hypothermia and hypotension may occur due to blockade of α_1-adrenergic receptors, especially in cats undergoing general anesthesia. Acepromazine combinations should be used with caution in hypovolemic and in hypotensive patients. Acepromazine has some antihistaminic effects and should not be administered to patients undergoing intradermal skin testing.

Agonists of α_2-adrenergic receptor combinations

Agonists of α_2-adrenergic receptors provide sedation, muscle relaxation, analgesia and chemical restraint in a dose-dependent manner.[65] They can produce emesis, especially when administered alone, due to direct stimulation of the chemoreceptor trigger zone (more commonly after xylazine).[33] Vomiting becomes an issue in cats with increased intraocular and intracranial pressures, with a detrimental impact on patient health and welfare. These drugs cause peripheral vasoconstriction, hypertension with reflex bradycardia and decreases in cardiac output. For this reason, agonists of α_2-adrenergic receptors are mostly reserved for cats with stable hemodynamic function. Hypothermia can occur via depression of the hypothalamic thermoregulatory center and the lack of muscle activity during PSA.

Acepromazine should not be used for PSA in cats with hypovolemia or dehydration, or in procedures with high risk of bleeding.

Dexmedetomidine and medetomidine are selective agonists of α_2-adrenergic receptors and should be preferred over xylazine. Xylazine should not be administered to systemically ill, pediatric or senior cats. Dexmedetomidine is the active isomer of medetomidine and twice as potent. Dexmedetomidine–butorphanol is a popular drug combination for PSA with a short onset of action (approximately 5 mins).[46] This combination provides superior sedative effects and a lower prevalence of vomiting than dexmedetomidine–buprenorphine during PSA for diagnostic imaging (ultrasound examination, radiography, CT), blood sampling, minor wound care and chemotherapy treatment administration.[48] However, studies have shown that the analgesia produced by dexmedetomidine–buprenorphine is superior.[66,67] The thermal antinociceptive effects of dexmedetomidine were enhanced when the drug was combined with buprenorphine.[68] The addition of ketamine (3 mg/kg) to dexmedetomidine (5 µg/kg) and butorphanol (0.3 mg/kg) increased the median duration of action for blood sampling by approximately two-fold. However, sedation scores were not different when compared with dexmedetomidine–butorphanol alone.[69]

Dexmedetomidine combinations usually decrease ejection fraction and fractional shortening, and increase end-diastolic and end-systolic volume in cats. This may affect the interpretation of echocardiography results. These combinations (eg, midazolam–butorphanol–dexmedetomidine or ketamine–dexmedetomidine) decrease cardiac output (approximately 50%), significantly more so than ketamine–midazolam–butorphanol (34%).[23] In contrast, medetomidine alone has been shown to increase afterload and was able to attenuate signs of dynamic left ventricular outflow tract obstruction in cats.[70] This is the reason why some veterinarians use low-dose medetomidine combinations for sedation in cats with HCM. Cardiac output is predominantly maintained via heart rate rather than contractility in the pediatric patient (cats <4 months of age). Administration of any α_2 receptor agonist in pediatric cats can severely reduce cardiac output and tissue perfusion and requires caution. Similarly, these drugs should not be administered to patients with life-threatening brady-arrythmias (eg, bradycardia secondary to urinary obstruction).

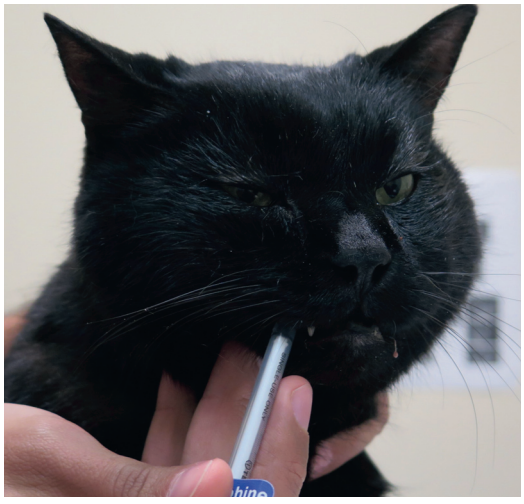

Figure 5 Oral transmucosal (buccal) administration of dexmedetomidine and buprenorphine can provide 'hands-off' sedation, analgesia and chemical restraint. Palatability is generally acceptable. Drug absorption is by the transmucosal route, assuming the drug is not spilled or swallowed by the cat

The oral transmucosal (buccal) route of administration has been used with medetomidine or dexmedetomidine as an alternative to intramuscular (IM) injections in cats.[57,71] The drug is injected with a 1 ml syringe into the cheek pouch to avoid oral administration (ie, drug swallowing) (Figure 5). Dexmedetomidine (40 µg/kg) in combination with buprenorphine (0.02 mg/kg) produced chemical restraint in cats when drugs were administered either buccally or IM. Sedative effects were not different between the groups. However, IM dosing produced superior sedation compared with buccal dosing when lower doses of dexmedetomidine (20 µg/kg) were used with buprenorphine.[57]

Antagonists of α_2-adrenergic receptors (atipamezole for dexmedetomidine and medetomidine; yohimbine for xylazine) can be administered IM to hasten recovery and antagonize potential adverse effects. Analgesia and muscle relaxation will also be antagonized. Atipamezole is typically administered IM at equal dose volume as the dexmedetomidine (0.5 mg/ml) or medetomidine volume. When using dexmedetomidine at 0.1 mg/ml concentration, the volume of atipamezole should be reduced to one-fifth of the dexmedetomidine dose volume. To reverse xylazine, administer 0.025–0.05 mg/kg of yohimbine IV slowly (25% of the published total dose), with the remaining 75% of the dose administered IM. This technique can help minimize yohimbine's unwanted side effects (ie, excitement and hypotension). Note that the use of anticholinergics with agonists of α_2-adrenergic receptors is normally contraindicated (see box).

Are anticholinergics indicated for the management of α_2 agonist-induced bradycardia?

Cardiovascular effects associated with agonists of α_2-adrenergic receptors are often biphasic. Phase 1 includes an increase in systemic vascular resistance (vasoconstriction) followed by an immediate reduction in heart rate (reflex bradycardia) with an overall increase in arterial blood pressure. During this phase, the administration of an anticholinergic (atropine or glycopyrrolate) is usually contraindicated. Tachycardia following the administration of an anticholinergic with concurrent vasoconstriction can result in severe hypertension with deleterious effects on vital organs such as the kidneys and brain. Tachycardia also increases myocardial oxygen consumption and reduces diastolic time, thus reducing ventricular filling time. The overall effect reduces stroke volume and predisposes the patient to myocardial ischemia. Phase 2 includes centrally mediated bradycardia; however, systemic vascular resistance often returns to normal, resulting in an overall decrease in arterial blood pressure. It is only during this phase (bradycardia and hypotension) that anticholinergics may be warranted.

Benzodiazepine combinations

The administration of benzodiazepines inconsistently produces sedation, and more commonly results in a transient period of excitement in adult, healthy cats. Patients may actually show signs of paradoxical aggressive and defensive behaviors.[23,72] There is generally a clinical impression that benzodiazepines cause minimal cardiovascular depression, but in one early study doses of 0.1 mg/kg of diazepam reduced systolic blood pressure and cardiac contractility, potentially because of the presence of propylene glycol in the formulation.[73] Nevertheless, midazolam and diazepam may be used for coinduction after the administration of propofol for endotracheal intubation in systemically ill cats. Benzodiazepines enhance the affinity of the neurotransmitter gamma-aminobutyric acid ($GABA_A$) for its receptor and have a synergistic effect with barbiturates, propofol and alfaxalone. Doses as low as 0.2 and 0.3 mg/kg of midazolam and diazepam, respectively, may have a propofol-sparing effect.[59]

In the authors' experience, midazolam–opioid combinations can be used in senior or critically ill cats (see top-right box on page 1035) to produce sedation for minor diagnostic procedures. Benzodiazepines are also used in combination with ketamine (see below). Diazepam should not be administered IM because the drug is hydrophobic and contains propylene glycol, which causes pain at injection; midazolam is water soluble and recommended for injectable PSA protocols. Flumazenil (0.01–0.04 mg/kg) is the antagonist of benzodiazepines.

Ketamine-based combinations

Ketamine, an N-methyl D-aspartate (NMDA) antagonist, causes dissociation between the thalamo-neocortical and limbic systems.[74] It is used as an adjunct analgesic in patients with hyperalgesia or central sensitization,[75] and can be administered IV, IM or buccally in cats.[76–78] In humans, ketamine used at subanesthetic doses (<1 mg/kg) rapidly decreased the perception of severe, acute pain and provided an opioid-sparing effect.[79,80] Its ability to produce similar analgesic effects at low doses is yet to be determined in cats.[81] This drug is known for causing 'emergence phenomenon' (dysphoria during recovery) in a variety of species, including humans, although it is not routinely seen with subanesthetic doses in cats (<0.5 mg/kg).[81] Ketamine is always administered in combination with sedatives and analgesics. The swallowing reflex is well maintained, but the risk of aspiration is still present.[82]

Ketamine-based protocols are used to produce chemical restraint for PSA (Table 4). The drug must be combined with a muscle relaxant (ie, midazolam or an agonist of α_2-adrenergic receptors) to prevent muscle rigidity, seizure activity and hypersalivation. The drug has an acidic pH and may cause pain during IM injection.[50] For this reason, appropriate physical restraint is required for the administration of ketamine combinations. Ketamine has the potential to increase heart rate via increases in sympathetic tone and should be avoided in patients with HCM or tachyarrhythmias.

Ketamine must be combined with a muscle relaxant agent to prevent muscle rigidity, seizure activity and hypersalivation.

Tiletamine–zolazepam and combinations

Tiletamine–zolazepam is available as a white powder combination (500 mg combined) and is reconstituted with 5 ml of sterile water to produce a 100 mg/ml solution. Alternatively, tiletamine–zolazepam powder can be reconstituted with 100 mg of xylazine and 400 mg of ketamine and administered IM at 3.3 mg/kg to cats for anesthesia. Following reconstitution, any unused drug should be discarded after 7 days when stored at room temperature or after 56 days when refrigerated.

This drug combination is widely used in feline practice for PSA and surgery. Sympathetic stimulation is observed after drug administration due to central nervous system stimulation, depression of baroreceptors and inhibition of norepinephrine (noradrenaline) uptake at adrenergic nerve endings.[83] Tiletamine–zolazepam can produce muscle rigidity, myoclonus, salivation, respiratory depression and prolonged recovery from anesthesia, which is a potential concern for patient welfare.[84] The combination of low doses of tiletamine–zolazepam with methadone provided superior sedation to acepromazine–methadone in healthy cats before neutering (Table 4).[37] Similar to ketamine combinations, tiletamine–zolazepam combinations should be avoided in cats with HCM.

Alfaxalone and combinations

Alfaxalone is a synthetic neurosteroid anesthetic drug that has been studied for PSA in cats.[24,41,42] The sedative and cardiorespiratory effects of alfaxalone have been evaluated when the drug was administered alone or in combination with butorphanol, hydromorphone or dexmedetomidine (Table 4). These protocols are versatile with a wide margin of safety and used for various procedures in combination with opioids (Table 4). Hypoventilation is a potential adverse effect of alfaxalone use in cats.[85] Some studies have reported ataxia, excitement and hyper-reactivity in some individuals during the recovery phase when doses of 5 mg/kg were used;[43] these effects may be attenuated by the administration of acepromazine and butorphanol.[86]

Alfaxalone-based protocols may involve large-volume IM injections. For example, a dose of 5–10 mg/kg may require 2–5 ml of volume administration. Cats may react to the injection even after sedation with dexmedetomidine–butorphanol.[43] The high volume produces discomfort and violent reactions at injection when administered at 10 mg/kg.[43] Other studies have reported that IM injections are normally tolerated when low doses are used (2 mg/kg).[46] The quality of anesthetic recovery is also a concern with alfaxalone.[87] Studies have reported cats thrashing, paddling, trembling and pacing in the cage.[43,87] Jurox, the manufacturer of Alfaxan Multidose, reports that repeated, supraclinical doses (25 mg/kg) of the product administered IV q48h for three doses does not result in adverse effects in cats.[88]

Propofol

The phenolic compound propofol is used as an anesthetic induction agent and, in some cases, for maintenance of anesthesia (total IV anesthesia). Propofol is sometimes administered as small boluses for PSA but it can induce adverse effects, especially in systemically ill cats. The drug produces dose-dependent cardiorespiratory depression with variable changes in heart rate, decreases in cardiac contractility and respiratory rate, hypoxia, hypercapnia and vasodilation.[52,89–93] Although hypotension may be observed following propofol administration, it is often mild in healthy cats.[92] Apnea may occur, especially after rapid bolus administration.[89,94–96] Caution is required when using propofol for PSA in patients with respiratory compromise and oxygen supplementation should be provided.

Small doses of propofol (1 mg/kg) may induce light sedation with signs of excitement and increased muscular activity in healthy cats (ASA PS I or II) sedated with acepromazine–methadone.[59] In contrast, these doses have been shown to induce smooth and mild sedation in critically ill cats with urinary obstruction requiring PSA for urethral catheterization after sedation with a midazolam–opioid combination.[97] Indeed, benzodiazepines may reduce propofol requirements for endotracheal intubation by 35% in healthy cats sedated with acepromazine–methadone[59] and by 26% in unpremedicated cats.[98]

Caution is required when using propofol for PSA in patients with respiratory compromise and oxygen supplementation should be provided.

The development of Heinz bodies after a 30-min infusion of propofol has been reported in cats, but only following the third day of administration;[99] after 7 consecutive days of these 30-min infusions, hemolysis was not detected.[99] The concern for Heinz body development associated with propofol administration in cats is, as yet, undetermined, as it does not appear to have clinical significance even following 24-h propofol infusions.[93]

PropoFlo 28 (Zoetis) contains 20 mg/ml of benzyl alcohol, a bacteriostatic preservative that requires glucuronidation for metabolism, and is a multiuse formulation of propofol with a 28-day shelf life. Excessive quantities of benzyl alcohol (>156 mg in 6.5 h) may cause central nervous system toxicity and potentially death.[100] For a standard 3 kg cat, an extreme overdose of propofol (approximately 26 mg/kg) would be required to produce these adverse effects.

Monitoring during PSA

Appropriate monitoring prevents, detects and aids in the treatment of complications such as hypoxia, hypoventilation and apnea, hypothermia, bronchospasm, cardiovascular depression, post-sedation delirium, prolonged recovery, vomiting and aspiration.[4,9,101] The American College of Veterinary Anesthesiology and Analgesia (ACVAA) has published guidelines for monitoring of patients undergoing sedation (see box).

Practical monitoring for patients undergoing PSA

Ventilation
- Respiratory rate
- Respiratory pattern
- Capnography

Circulation
- Capillary refill time
- Arterial blood pressure
- Pulse rate, rhythm and quality

Oxygenation
- Mucous membrane color
- Pulse oximetry

Thermoregulation
- Rectal or axillary temperature

Pain
- Feline Grimace Scale
- Glasgow Feline Composite Pain Scale
- Short-form UNESP-Botucatu multidimensional composite pain scale

- Perform cardiopulmonary auscultation
- Have means of oxygen supplementation to hand
- Endotracheal tube and materials for IV catheterization should be readily available
- If patient loses control of protective airway reflexes, monitoring for general anesthesia should begin immediately

Adapted from ACVAA guidelines: acvaa.org/wp-content/uploads/2019/05/Small-Animal-Monitoring-Guidlines.pdf

✣ **Routine neurological assessment** (menace response, nystagmus, palpebral reflex, response to stimuli) monitors the depth of sedation.

✣ **Pulse oximetry** (SpO_2) is a valuable monitoring tool during the sedation and recovery periods. Transmission SpO_2 probes placed on the tongue, pinna or a (non-pigmented) toe can provide an early indication of respiratory complications and can significantly reduce the risk of mortality (Figure 6).[3] Failure to monitor oxygen saturation during sedation and anesthesia also increased the risk of death.[2] In patients receiving high levels of fractional inspired oxygen (FiO_2), pulse oximetry can be misleading because desaturation may not be apparent until a patient is truly hypoxemic. Note also that pulse oximetry values may be affected by or unattainable with the administration of α_2-adrenergic agonists (eg, dexmedetomidine or medetomidine).

✣ **Capnography** is often not employed because patients are not routinely intubated during PSA. However, a side stream adapter can be placed close to the patient's nostrils to estimate end-tidal carbon dioxide values and monitor ventilation (Figure 6).

✣ **Non-invasive blood pressure monitoring** using techniques such as oscillometry or Doppler ultrasound and sphygmomanometry is a cost-effective and simple method for indirect assessment of perfusion. The Doppler provides an audio, real-time pulse for rate and rhythm evaluation. Obesity may impact Doppler probe blood pressure readings from the coccygeal and radial artery.[102] There is potential for Doppler measurements to more closely resemble mean arterial pressure in cats.[103] Regardless, blood pressure trends associated with heart rate and oxygenation are the most important outcome for monitoring when using these devices.

Recovery procedures

The quality of recovery is dependent on body temperature, duration of the procedure, drug antagonism (whether performed and/or effective), pain, and patient health status and behavior. Complications may arise during the sedation period; however, the majority of fatalities (52–60%) have been reported to occur within the first 3 h after the procedure has ended.[2,5]

Prolonged hypothermia and emergence, collapse and/or excitement may occur during recovery.[9] This is particularly true when anesthetics are administered for PSA. Post-procedure excitement or delirium can be controlled with dexmedetomidine (0.5–1 µg/kg IV) administered slowly for re-sedation in a quiet environment away from other animals. Management and prevention of hypothermia during PSA was discussed earlier (see section on 'patient assessment preparation before PSA') and the same principles apply during recovery. Reversal agents for opioids, benzodiazepines and α_2-adrenergic agonists should be readily available and administered in the event of prolonged emergence from PSA. Hypotension has been reported following the reversal of dexmedetomidine with atipamezole in isoflurane-anesthetized cats;[104] however, this should not be a concern during PSA. Monitoring should continue for a minimum of 3 h following completion of the procedure and animals should not be left unattended for long periods of time until they have recovered.

Patients are considered fully recovered when they are responsive to normal stimuli, have regained protective airway reflexes and are able to maintain normal cardiopulmonary parameters. Some cats may require continuous monitoring and oxygenation (eg, oxygen tent or chamber). If intubation was necessary, extubation is recommended when a convincing swallowing reflex is present; cats should be monitored for laryngospasm and upper airway obstructions following extubation. A small amount of water and food can be offered to patients that are awake and standing with minimal to no ataxia.

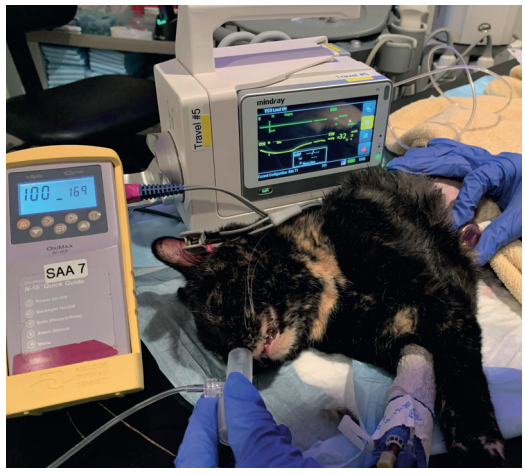

Figure 6 **Capnography (performed using a side-stream adapter), pulse oximetry and cardiac auscultation in a cat undergoing procedural sedation and analgesia for an abdominal ultrasound examination.** *Courtesy of Mary T Schacher*

Complications may occur during the sedation period; however, the majority of fatalities have been reported to occur within 3 h after the end of the procedure.

KEY POINTS

- Feline patients often require PSA in veterinary practice for various procedures.
- Complications may arise, especially when risk factors are present.
- The choice of drug protocol depends on the procedure and the health status of the patient, including any concomitant diseases.
- The need for analgesia dictates the type of opioid to be administered.
- The results of clinical and experimental trials are difficult to extrapolate to every case, and an individualized approach to PSA should be taken.
- Monitoring, fluid therapy and good practices, as discussed in this article, are paramount for successful PSA in cats.

Conflict of interest

Dr Paulo Steagall has provided consultancy services to Boehringer Ingelheim, Dechra Pharmaceuticals, Elanco, Procyon and Zoetis; has acted as a key opinion leader to Boehringer Ingelheim, Dechra Pharmaceuticals, Elanco, Vetoquinol and Zoetis; and has received speaker honoraria from Boehringer Ingelheim, Dechra Pharmaceuticals, Elanco and Zoetis.

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Ethical approval

This work did not involve the use of animals and therefore ethical approval was not necessarily required.

Informed consent

This work did not involve the use of animals and therefore informed consent was not required. For any animals or humans individually identifiable within this publication, informed consent (either verbal or written) for their use in the publication was obtained from the people involved.

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