Premedication with alpha-2 agonists – procedures for monitoring anaesthetic

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Lisa Angell RVN, VTS(Anaesthesia), **looks at the benefits, dosing requirements, alpha-2 agonist options and best practice around premedicating small animal patients in veterinary anaesthesia**

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PREMEDICATION administered before general anaesthesia is widely used in veterinary practice and may be achieved by using a single drug or a combination.

Beneficial effects

Premedication has several beneficial effects, including:

Sedation

Many patients become stressed in a hospital environment. Using a sedative as part of a premedication protocol reduces anxiety and stress for the patient and anaesthetist, and minimises the restraint necessary to place an intravenous catheter.

A patient stressed at induction of anaesthesia has higher concentrations of circulating catecholamines (adrenaline and noradrenaline); this is important because some anaesthetic drugs can sensitise the heart to the effects of catecholamines and make cardiac arrhythmias more likely

to develop. A sedated animal is less stressed and therefore has less catecholamine release.

Analgesia

Depending on the reason for general anaesthesia, many patients need an analgesic drug in the premed. If an animal is already in pain, or if the procedure is painful, providing analgesia is essential. Moreover, giving analgesics before tissue damage occurs (if possible) may help to reduce peripheral and central sensitisation and, consequently, pain after surgery may be less severe. This is termed “pre-emptive” analgesia. Some analgesic drugs also provide some sedation, although this may not be enough to reduce stress and anxiety in all patients.

Reduced doses of anaesthetic drugs needed for induction and maintenance

A carefully chosen premedication protocol not only reduces the doses of anaesthetics needed for induction and maintenance, but also helps to “smooth out” the whole process of anaesthesia, so changes in depth associated with different levels of surgical stimulation are less dramatic. Dose reduction also lessens the dose-dependent cardiovascular and respiratory depression typically seen when using most anaesthetic agents.

Smooth recovery

The effect of many of the drugs commonly used for premedication lasts into the recovery period and helps keep patients calm during recovery from anaesthesia. A patient that recovers quickly from anaesthesia may become stressed or anxious. If the premedication has worn off, these drugs can be “topped up” before the end of anaesthesia to aid a smooth recovery.

What are alpha-2 agonists and why are they useful drugs for premedication?

Alpha-2 agonists are primarily sedative drugs with the added benefits of reducing anxiety, and provide some analgesia and muscle relaxation. Xylazine, medetomidine and dexmedetomidine are licensed in the UK for small animal use.

Xylazine was the first to be used in veterinary practice, followed by medetomidine and more recently, dexmedetomidine. Xylazine is relatively non-selective for alpha-2 receptors, whereas medetomidine and dexmedetomidine have much greater selectivity. Stimulation of alpha-1 receptors in the heart by xylazine might explain its reduced cardiovascular safety compared with medetomidine and dexmedetomidine[1].

Medetomidine is an equal mixture of two optical isomers – dexmedetomidine and levomedetomidine. The dextrorotatory isomer is the active ingredient, providing sedation and

analgesia, whereas levomedetomidine is largely inactive.

Since 2007, dexmedetomidine has been available for clinical use in dogs and cats, with reported benefits of increased duration of analgesia[2] and a reduced requirement for drug metabolism as only the active isomer is used. This might be beneficial when an anaesthetic protocol includes a number of drugs, all of which may require hepatic metabolism. The use of dexmedetomidine reduces hepatic workload and, potentially, the risk of drug interactions and delayed recoveries[3].

The analgesia produced by alpha-2 agonists is similar to, and synergistic with, that produced by opioids[4]. Anecdotally, alpha-2 agonists may be more effective in relieving “visceral” pain (for example, associated with ovariohysterectomy) than “somatic” pain (for example, associated with musculoskeletal injury).

In the CNS, alpha-2 receptors are found in high numbers both pre and postsynaptically on nociceptive neurons in the dorsal horn of the spinal cord. They are also found in some areas of the brain stem – all these areas are involved in the modulation of nociceptive neurotransmission (pain transmission pathways).

The effects of alpha-2 agonists are seen within five minutes of intravenous administration, but it can take up to 20 minutes to see maximal sedation if they are given intramuscularly. Sedation is profound and dose-related, and data sheet doses tend to be higher than those commonly used in practice.

What are the benefits of using dexmedetomidine premedication?

The benefits of using dexmedetomidine premedication are:

- **Reliable sedation.** Dexmedetomidine provides reliable, dose-dependent sedation, which is extremely beneficial in stressed or aggressive patients to smooth their induction to anaesthesia.
- **Analgesia.** Dexmedetomidine provides analgesia (as discussed previously) and can form part of a multimodal approach to good pain relief. Dexmedetomidine can also be administered via intravenous infusion at “micro” doses to control pain, although such use is off-label[5].
- **Reduction of anaesthetic agent requirements.** This reduces the dose-dependent cardio-respiratory side effects of induction and maintenance agents (see section on how to administer general anaesthetic drugs).
- **Smooth recovery.** Patients with dexmedetomidine “on board” during the recovery period usually regain consciousness with less “angst” and excitability.
- **Reversibility (antagonism).** The effects of dexmedetomidine are completely reversible with atipamezole if required. With the doses we use clinically, we rarely reverse dexmedetomidine premedication as patients benefit from smoother recoveries and the extra

analgesia.

Monitoring the patient in recovery should be continuous. Remember, if you reverse dexmedetomidine's sedation, you also reverse the analgesia it provides.

What are the caveats when using dexmedetomidine for premedication?

All alpha-2 agonists can have marked effects on the cardiovascular system and are most suitable for sedation or premedication in animals with a normally functioning cardiovascular system. Urine production is increased due to inhibition of vasopressin secretion, which is of limited clinical significance in healthy animals, but may be a problem in those patients with "blocked bladders". Dexmedetomidine can be used once the blockage is removed.

Alpha-2 agonists reduce liver blood flow and consequently reduce the rate of hepatic metabolism of other drugs. In a healthy patient this is of little concern, but may be more significant in animals with liver disease. Care should be taken when using alpha-2 agonists in diabetic patients as they inhibit insulin secretion from the pancreas and can cause hyperglycaemia.

Although alpha-2 agonists provide analgesia, this is of shorter duration than the sedative effects and these drugs used alone do not provide sufficient analgesia for surgical procedures. With this in mind, alpha-2 agonists are most commonly used in combination with opioids to produce synergistic analgesia and sedation, thus allowing doses (and consequently the side effects) of both drugs to be reduced (see Table 1 for dexmedetomidine premedication doses).

How should we administer general anaesthetic following dexmedetomidine premedication?

Doses of drugs used for induction are often dramatically reduced and consequently they should be given slowly and to effect. For example, the typical dose of propofol is calculated at a dose rate of 4mg/kg; when using dexmedetomidine, propofol requirements can sometimes be reduced to as little as 1mg/kg to achieve intubation[4].

Slow injection is essential because all alpha-2 agonists increase the circulation time from the injection site to the brain, so it can take longer to see the full effect of any given dose. It is important to remember when dexmedetomidine has been used in premedication relative overdose at induction can occur if too much intravenous agent is given, or if it is injected too quickly.

The concentration of inhalant agent required for maintenance of anaesthesia is similarly reduced – sometimes by as much as 70 per cent when using isoflurane[1]. As a result, lower vaporiser settings are usually required.

How should I monitor a patient administered a dexmedetomidine premedication?

In terms of monitoring a patient that is administered a dexmedetomidine premedication, it is necessary to understand the physiological changes that occur following administration of dexmedetomidine.

All alpha-2 agonists cause an initial arterial hypertension because of intense peripheral vasoconstriction and, thus, an increase in systemic vascular resistance. This is mediated via stimulation of alpha-2 receptors in the peripheral arterioles. The arterial hypertension activates the baroreflex (mediated by baroreceptors in the aorta and carotid sinuses), thus reducing heart rate in an attempt to normalise the patient's arterial blood pressure. Arterial pressure generally returns to normal levels, but due to reduced release of catecholamines, it might fall slightly below normal[6].

In contrast, acepromazine has the opposite effect on blood vessels as it causes vasodilation, meaning arterial blood pressure may fall if not supported by intravenous fluid therapy. You may also see an increase in heart rate; this is a compensatory reflex as the sympathetic nervous system increases the heart rate in response to the reduction in arterial blood pressure.

Heart rate

The most noticeable effect of dexmedetomidine is bradycardia. In dogs, it is expected to see heart rates of 45 to 60 beats per minute and in cats, 80 to 100 beats per minute, which is consistent with a typical 50 per cent reduction compared to pre-sedation values. However, this is a normal physiological response to dexmedetomidine and is usually well-tolerated in healthy animals.

Electrocardiogram

If your patient is connected to an electrocardiogram, typical arrhythmias to look out for include first and second degree atrioventricular block (Figure 1). This is really an extension of the sinus bradycardia and can be tolerated as long as heart rate and arterial blood pressure are not excessively low. If this is not the case, treatment with atipamezole is indicated. Anticholinergic therapy (for example, with atropine) is controversial because a heart that is beating faster against a higher vascular resistance increases arterial pressure even more and has to work harder, with a consequent increase in oxygen demand.

Pulse oximeters

Pulse oximeters are probably the most common monitoring devices used in veterinary anaesthesia. They are simple to use, but it is very important to understand how they work and how to interpret the information they provide. The pulse oximeter measures transmission of light through a pulsatile

vascular tissue bed (for example, tongue, toe) and consists of two light emitting diodes (red and infrared), a photocell detector and a microprocessor with a visual display unit.

The data is analysed and displayed as a percentage of the total amount of haemoglobin that is saturated with oxygen (SpO_2). The SpO_2 is rarely affected when using dexmedetomidine; however, vasoconstriction can make it harder for the machine to give an accurate value because the data analysis depends on adequate pulsation of tissues.

Also, sinus arrhythmia may be more pronounced after use of dexmedetomidine; this benign variation in heart rate occurs during the breathing cycle, where the heart rate increases during inspiration and decreases during expiration and the expiratory pause. This variation can confuse a pulse oximeter and you may see “jumping” of the pulse rates as it tries to “count” the pulses over a certain time frame. It is important not to rely on this to give you an accurate pulse/heart rate; instead, rates should be taken directly from the patient using a stethoscope, palpation of pulses and/or listening to a Doppler flow signal.

Mucous membranes

Peripheral vasoconstriction explains why patients often appear “pale” or mildly cyanotic in colour; while this would be abnormal when using other premedication drugs (for example, acepromazine), it is more commonly seen when using dexmedetomidine.

Arterial blood pressure

Arterial blood pressure is usually measured non-invasively using either an oscillometer or a Doppler machine. Oscillometers normally work well on patients weighing more than 10kg; however, the vasoconstriction caused by dexmedetomidine means these devices sometimes fail to give readings, which can be mistaken as hypotension.

In smaller patients, the use of a Doppler to monitor blood pressure is more reliable; the Doppler probe is placed over a peripheral pulse, although due to vasoconstriction in the periphery the signal may be reduced, which can sometimes make it difficult to get accurate results (Figure 2).

Respiration

Alpha-2 agonists can cause dose-dependent respiratory depression, but at therapeutic doses, normal arterial partial pressures of oxygen and carbon dioxide are usually maintained without intervention (for example, intermittent positive-pressure ventilation). Capnography can be used as normal to ensure adequate ventilation and cardiac output.

Monitoring body temperature

Although alpha-2 agonists have a direct depressant effect on the thermoregulatory centre, peripheral vasoconstriction tends to reduce heat loss. However, if patients do get cold, the vasoconstriction can make it more difficult to warm them up because it is more difficult to transfer heat from the periphery to the core (Figure 3). Temperature should be monitored as soon as premedication is given because patients can lose heat during the period between premedication and induction of anaesthesia.

The way in which we monitor patients during anaesthesia following premedication with an alpha-2 agonist should be no different to any other anaesthetic case. As long as you are aware of the effects these drugs have on the body systems and what monitoring equipment works best, alpha-2 agonists can help provide a very smooth, stress-free anaesthetic and recovery.

References

- 1. Seymour C and Duke-Novakovski T (2007). *BSAVA Manual of Canine and Feline Anaesthesia and Analgesia* (2nd edn), BSAVA, Gloucester.
- 2. Murrell J C and Hellebrekers L J (2005). Medetomidine and dexmedetomidine: a review of cardiovascular effects and antinociceptive properties in the dog, *Veterinary Anaesthesia and Analgesia* **32**(3): 117-127.
- 3. Bryant S (2010). *Anaesthesia for Veterinary Technicians* (1st edn), Wiley-Blackwell, Ames, IA.
- 4. Dugdale A (2010). *Veterinary Anaesthesia: Principles to Practice*, Wiley-Blackwell, Ames, IA.
- 5. Valtolina C, Robben J H, Uilenreef J et al (2009). Clinical evaluation of the efficacy and safety of a constant rate infusion of dexmedetomidine for postoperative pain management in dogs, *Veterinary Anaesthesia and Analgesia* **36**(4): 369-383.
- 6. Pypendop B H and Verstegen J P (1998). Haemodynamic effects of medetomidine in the dog: a dose titration study, *Veterinary Surgery* 27(6): 612-622.

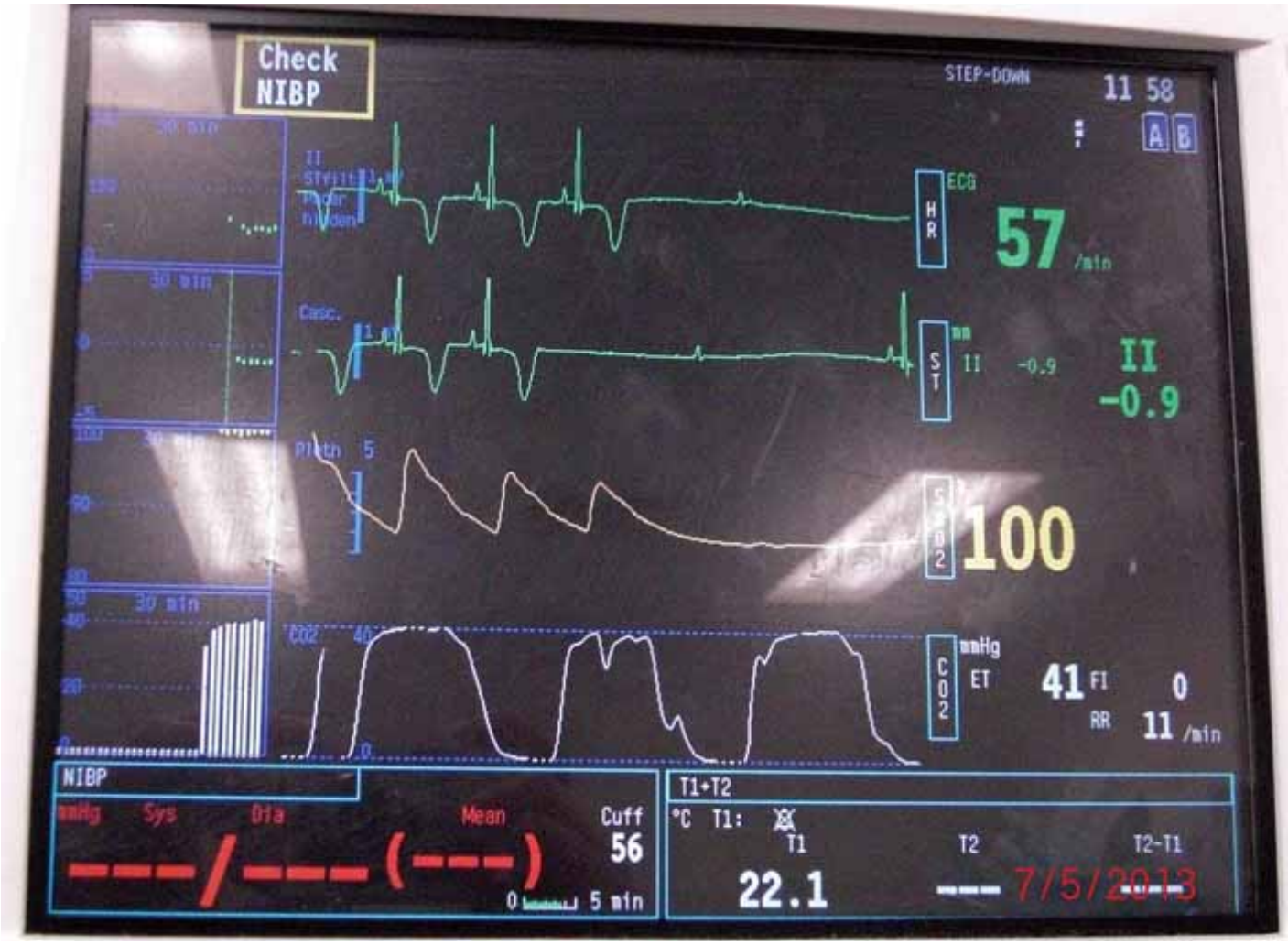

Figure 1. The electrocardiogram trace shows second-degree atrioventricular block – an arrhythmia commonly seen following dexmedetomidine administration.

Figure 2. A Doppler machine is used to monitor arterial blood pressure during anaesthesia following dexmedetomidine premedication.

Figure 3. Following premedication, the patient’s temperature can be monitored and maintained with a warming device.

	Intramuscular	Intravenous
Dog	2.5μg/kg to 10μg/kg (sole agent) 2.5μg/kg to 5μg/kg (with opioid)	1μg/kg to 5μg/kg
Cat	2.5μg/kg to 10 μg/kg (sole agent) 2.5μg/kg to 5μg/kg (with opioid)	1μg/kg to 5μg/kg
		Doses are off label

TABLE 1. Dexmedetomidine premedication doses