HKSTP IACUC

07 – General Anesthesia, Analgesics and Sedatives of Laboratory Animals Guidelines

Version History

Version	Effective Date
1	28/02/2023

1. Purpose

The guidelines aim to provide a reference to the minimum standard required when anesthetizing laboratory animals. Please note that requirements for anesthesia of animals for specific species may differ according to the species' physical structure.

2. General Principles

2.1 All anesthesia regimen must be reviewed by HKSTP IACUC to ensure standards of animal welfare.

2.2 All anesthesia regimen must be performed in appropriate spaces that have been approved by HKSTP IACUC. The space must be equipped with appropriate scavenging system for removal of waste gases and adequate ventilation for human safety.

2.3 Anesthesia regimen should be designed to allow animals to gradually recover and not cause injury to themselves or to other surrounding animals.

2.4 Physiological parameters and anesthetic depth of animal should be regularly monitored throughout and during the anesthesia process as well as during anesthetic recovery.

2.5 Animals under anesthesia and until they have fully recovered should not be left unsupervised.

2.6 Details of each animal and their respective anesthesia processes should be recorded regardless of procedure type.

2.7 Appropriate supportive care should be provided.

2.8 It is the Principal Investigator's responsibility to ensure that personnel carrying out any procedures involving anesthesia are equipped with adequate knowledge and training.

3. General Anesthesia, Analgesics and Sedatives [Rodent Specific]

3.1 Fasting prior to anesthesia is usually not necessary for mice and rats as they do not vomit. In cases where fasting prior to anesthesia is required, the fasting period shall be limited to no more than two to three hours due to the high metabolic rate of small rodents. Ad libitum access to clean drinking water must be provided unless scientifically justified.

3.2 As hypothermia is the most common cause of postprocedural/surgical mortality, measures to prevent heat lost and maintain animals' body heat during surgery is highly recommended.

3.3 Heating pads or warm water bottles wrapped by an insulating material can be used to eliminate hot spots to prevent burns.

3.4 Heat lamps via indirect beam on animal. The heat lamp may reflect off a metal surface and place the animal in the reflected beam.

4. Recommended Types of Anaesthestics, Analgesics and Sedatives [Rodent Specific]

4.1 Inhalation Anaesthestics

i. **Isoflurane** – should be delivered via a precision vaporizer to achieve isoflurane in concentration of 1-3% in oxygen (up to 5% for initial induction).

4.2 Injectable Anaesthetics

i. **Ketamine** – it is a dissociative anaesthetic often used in combination with other agents such as alpha2-agonists (e.g. xylazine and medetomidine) and benzodiazepines (e.g. midazolam and diazepam). Its advantages include wide margin of safety in most species and its NMDA receptor blocking action which can have analgesic effects. Disadvantages of ketamine includes some irritancy. It is also a Dangerous Drug in Hong Kong legislation Cap. 340, and controlled drug in other legislations.

ii. **Barbiturates** (e.g. Pentobarbital) – Pentobarbital is often used as an agent for euthanasia but can still be used for anaesthesia. It is most frequently used in terminal or acute studies as recovery can be prolonged and unpleasant. Pentobarbital can be an anaesthetic of choice when neurophysiological recordings such as visual or auditory responses are required.

iii. **Tribromoethanol** (e.g. Avertin) – Avertin is often used as an anesthetic for short (15-30minutes) surgical manipulations. The effects of tribromoethanol can be unpredictable, especially in young mice and rats aged 16 days or less, or in animals with altered carbohydrate metabolism. Tribromoethanol is NOT recommended for repeated anesthesia.

4.3 Analgesia

i. **Opioids** (e.g. buprenorphine, butorphanol) – Opioids can be used with general anaesthetic protocol to provide pre-emptive analgesia when given 30 minutes prior to surgical incision, but more often it is used as post-surgical analgesics. Opioids can vary in their duration of effect as well as their analgesic properties. Buprenorphine is the longest-acting and is good for most post-operative applications. It is advisable to administer by injection as oral use requires a

much higher dose because of first-pass liver metabolism when absorbed from the gut. Other opioids that are full agonists may produce respiratory depression, but buprenorphine and butorphanol are mixed agonists/antagonists at different opioid receptors.

ii. **Non-steroidal anti-inflammatory drugs (NSAIDs)** (e.g. meloxicam) – NSAIDs are effective to reduce inflammation and play a role in the multimodal analgesic protocol as it has an effect on the transduction and modulation of pain. Meloxicam may have a duration of analgesic action for up to 24 hours.

Disadvantages of NSAIDS include gastric upset and ulceration with prolonged use, there is also a possibility NSAID may decrease clotting ability. These undesirable effects are more likely with prolonged use, for most situations limit the use of NSAIDS to 3-4 days per animal, except with approved protocols or veterinary supervision. Prolonged use may also increase risk of kidney and liver disease, therefore it should not be used in dehydrated animals or animals with kidney or liver dysfunction.

iii. **Local anaesthetic/analgesic drugs** (e.g. lidocaine and bupivacaine) – Local anaesthetics is most applicable during surgery and post-operative use. Their analgesic effect blocks the transduction of pain at the peripheral level when applied locally at sufficient concentration. Local anaesthetic can be used in conjunct with general anaesthestic to provide additional post-surgical analgesia, however it should not be used alone to control post-surgical/post-procedural pain due to its short duration of action.

Application of local anaesthetics can provide additional pain relief in conjunction with general anaesthesia and can reduce the need for frequent redosing of opioids and/or NSAIDs. Local anaesthetics should not be given intramuscularly or intravenously as they can cause systemic toxicity can result from overdosage and may have a cardiovascular effect. Lidocaine may sting when first injected, it can be diluted with sodium bicarbonate in a 9:1 lidocaine to sodium bicarbonate ratio to decrease local irritation.

References

UBC Animal Care Committee: Guidelines on Anesthesia of Rodents. Revised 2018. https://animalcare.ubc.ca/sites/default/files/documents/Guidelines%20on%20Anesthesia%20of%20Rodents%202018_0.pdf