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# Rat-Specific Anesthesia Guidance

## I. Purpose:

This document has been designed by the ARC veterinary staff as a guideline for rat anesthesia. This is not intended to be an inclusive list of all possible drug combinations that can be used in rats. Instead, these guidelines are general recommendations. Consequently, they do not include reference to specific research-associated concerns. If you have questions about the use of anesthetics for your particular situation, please work with your area veterinarian to develop the most effective anesthetic plan.

Anesthesia is the loss of feeling in all or part of the body, with or without loss of consciousness. Animals may be anesthetized for surgery, for non-surgical procedures that may be painful, or for non-painful procedures that require immobilization. Steps must be taken before, during, and after anesthesia to ensure the safety of the animal and efficacy of anesthesia. These are listed in the General Guidelines section below.

Anesthetic drugs can be administered parenterally or by inhalation. Commonly used anesthetic agents are described below. The choice of anesthetic agent will depend on the procedure to be performed, research aims, and other factors such as animal age. Consult your area veterinarian with questions about drug selection.

## II. General Guidelines and Considerations for Rat Anesthesia:

- Acclimation: A one-week post-shipping acclimation period is recommended for all animals to prevent stress-induced responses. At a minimum, animals require 72 hours to regain basic physiological baselines.

- Fasting: Pre-anesthetic fasting is usually not necessary for mice due to their inability to vomit. However, if fasting is employed (e.g., to stabilize body weights before anesthesia) limit to no more than 2-3 hours due to the high metabolic rate of small rodents. **Never restrict water.**

- Eye protection: Rat eyes remain open under anesthesia. This can lead to corneal drying and trauma. Apply ophthalmic ointment (e.g., Paralube® or Lacrilube®) if:

- The anesthetic event lasts longer than 5 minutes.
- Anesthesia is being delivered by facemask.

- Monitoring: Regardless of the anesthetic administered, monitor rats under anesthesia to avoid excessive depression of cardiac and respiratory functions, or insufficient anesthesia.
  - Parameters that can be monitored in an anesthetized rats without specialized equipment include:
    - Anesthetic depth – toe pinch
    - Respiratory rate and pattern – normal undisturbed rate = ~70-120/min, a slow rate drop of 50% is acceptable during anesthesia
    - Mucous membrane color – should be pink not blue or grey
    - Body temperature can be monitored with a rectal thermometer and should be between 96.5 - 99.5°F.
    - Oxygen saturation (>95%) and heart rate (300-550 beats/min) can be monitored using a specialized rodent pulse oximeter.
    - Contact your area veterinarian with questions about monitoring or monitoring equipment.

- Heat support: All species are at risk for hypothermia while under anesthesia. Rats are particularly susceptible due to their high body surface area to body mass ratio. Hypothermia induces a significant physiological stress on animals that can prolong recovery and potentially be fatal.
  - Provide supplemental heat during all anesthetic events.
  - Supplemental heat sources include circulating water blankets, electric heating pads, and commercial products that can be warmed in a microwave or water bath (such as isothermic pads or gel warmers). Never place the animal directly on the heat source.
  - Contact your area veterinarian with questions about using or purchasing supplemental heat sources.

- Fluid support: Consider providing warm SQ or IP fluids, particularly for prolonged anesthetic events or animals that are ill, aged, or debilitated. Consult your veterinarian with additional questions.

- Recovery: Continue to monitor animals until they are fully recovered.

- Recover animals on paper towels (without bedding) in a clean cage. This minimizes the risk of tracheal obstruction or pneumonia.
- Recover anesthetized animals alone in a cage.
- Continue to provide supplemental heat during recovery.
- When the animal is ambulatory, return it to the home cage with immediate access to food and water.
- Depending on the surgery performed, mice may need to be housed individually in the post-operative period to avoid suture gnawing or incision-site trauma caused by cagemates. Any plans for individual housing should be included in the IACUC protocol so that they can be reviewed and approved.

## III. Anesthetic Drugs and Procedures:

1. **Inhaled Anesthetics:** Isoflurane is the preferred inhaled anesthetic. It has rapid and reliable onset and recovery.

   A. Inhalation anesthesia may be delivered by the drop jar method, or by induction chamber, facemask, or endotracheal tube using a precision vaporizer.

      **i.** Drop jar:
         a. Do not allow the rat to come into direct contact with the liquid inhalant anesthetic (which can be achieved by placing an impermeable mesh grid over the cotton/gauze).
         b. Because the anesthetic concentration cannot be controlled in the chamber and can rapidly reach toxic concentrations, this method is reserved for very short procedures such as subcutaneous tumor implantation, or induction prior to facemask anesthesia.

      **ii.** Induction chambers, facemasks and endotracheal tubes:
         a. These require gas anesthesia machines with an oxygen source and a precision vaporizer. Some research units may use room air rather than pure oxygen as a gas source which may also be acceptable.
         b. The vaporizer must be compatible with the specific inhaled anesthetic agent.
         c. Due to the small respiratory capacity in rats, use a non-rebreathing system.

      **iii.** When using inhalant anesthesia, use a fume hood or an anesthetic system equipped with a gas scavenging system to minimize occupational exposure to exiting gases.

| Drug | Dose | Oxygen flow rate | Comments |
|---|---|---|---|
| Isoflurane **Recommended** | 4-5% for induction 1-2% for maintenance | 300-600 ml/min | Approximately 0.6 mls pof liquid isoflurane per liter of chamber volume |

2. **Injectable Anesthetics:** Combined ketamine/xylazine is the preferred injectable anesthetic in rats. Other commonly used injectable agents are listed below.

    A. Rats vary significantly in their sensitivity to various anesthetics. Age, body composition, strain, health status, genetic manipulation, and sex are just a few of the factors that can contribute to anesthetic sensitivity. The following doses are general guidelines that may vary significantly based on the aforementioned factors.When adding anesthetics to your protocol, it is advisable to provide a range to allow titration for the specific needs of each animal.

    B. Intramuscular (IM) injections are not recommended in rats as complications such as tissue irritation, lameness and self-mutilation can result

| Drug | Dose | Route | Duration of Anesthesia | Comments |
|---|---|---|---|---|
| Ketamine + xylazine (Rompun®) | 40-90 mg/kg ket + 5-10mg/kg xyl. | IP, SQ | 45-90 minutes | Thermal support is crucial. If additional anesthetic is needed, supplement with 1/3 dose of ketamine only. Do not re-dose xylazine. |

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|---|---|---|---|---|
| | | | | Xylazine (20 mg/ml) can be reversed with 1 - 2 mg/kg yohimbine IP or a volume of atipamezole equal to the volume of Xylazine (20 mg/ml) given (IP)**. |
| Ketamine +Xylazine +Acepromazine | 75 -90 mg/kg ket + 5- 10 mg/kg Xy + 1-2 mg/kg Ace | IP, SQ | 60-120 minutes | Thermal support is crucial. To prolong anesthesia, supplement with 1/3 dose of ketamine only. Xylazine can be reversed with 1 - 2 mg/kg yohimbine IP or a volume of atipamezole equal to the volume of Xylazine (20 mg/ml) given (IP)**. |
| Ketamine + Dexmedetomidine | 75-90 mg/kg ket 0.5-0.75 mg/kg Dex | IP, SQ | 45-90 minutes | Thermal support is crucial. If additional anesthetic is needed, supplement with 1/3 dose of ketamine only. Do not re-dose dexmedetomidine. Dexmedetomidine can be reversed with a volume of atipamezole equal to the volume of Dexmedetomidine used** |
| Ketamine + diazepam (Valium®) | 40-80 mg/kg ket + 5-10 mg/kg dia. | IP | 20-30 minutes | |
| Pentobarbital (Nembutal®) | 40-60 mg/kg | IP | 80-90 minutes | Dose sufficient to produce surgical anesthesia may cause severe respiratory depression and death. Administer diluted in saline (<10 mg/ml). AVOID buprenorphine co-administration. Buprenorphine and Pentobarbital will result in cardiorespiratory depression. Administer buprenorphine after full recovery. |

* A good starting point is 100 mg/kg Ketamine and 7 mg/kg Xylazine

****** Atipamazole (5 mg/ml) is 10X the concentration of Dexmedetomidine (0.5 mg/ml). You need 4-6X as many mg of Atipamaozle (5 mg/ml) to reverse Dexmedetomidine. However, it also has a very high safety margin, so giving an equal volume of Atipamazole to Dexmedetomidine gives you 10 X as many mg of Atipamazole, it is safe, and it allows for reversal without calculating a dose if reversal is urgent. Equal volumes of Atipamaozle (5 mg/ml) to reverse small animal Xylazine (20 mg/ml) also works because even though Xylazine has a stronger concentration (20 mg/ml), Atipamazole (5 mg/ml) is cleaner and binds more tightly to the alpha 2 receptor, so equal volumes allows for reversal of xylazine (20 mg/ml) as well.

C. One type of injectable anesthetic is a local anesthetic.

**i.** Local anesthetics block nerve impulses by specifically binding the voltage-gated Na+ channel in the nerve cell membrane.

**ii.** Routes of administration include topical to mucus membranes (nose, eye, etc.) or injected directly into tissues and around nerve bundles.

**iii.** Administration of local anesthetics prior to the painful stimulus (eg. incision) would be considered an adjunct analgesic to opioid and NSAID analgesics.

**iv.** Use as a primary analgesic is discouraged due to the short duration (hours).

| **Drug** | **Dose** | **Route** | **Comments** |
|---|---|---|---|
| Lidocaine | 4 mg/kg (0.4 mL/kg of a 1% solution) | Local infiltration | Local infiltration Do not exceed 7 mg/kg total dose |
| Bupivacaine **Recommended** | 1-2 mg/kg (0.4-0.8 mL/kg of a 0.25% solution) | Local infiltration | Do not exceed 6 mg/kg total dose |

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