



Guidance on Analgesia in Research and Instruction Animals

Use of chemical analgesics, while not the only means of mitigating pain and distress, is often the most common and effective approach available in research settings.

Different classes of analgesics work via different mechanisms, and using multiple classes of analgesics simultaneously (multimodal analgesia) can be more effective than use of any one agent alone and can lower the dose required of any single drug.

Likewise, administering analgesics before initiation of pain/distress (preemptive analgesia) can increase the effectiveness of the analgesics given and can lower the dose required of any single drug.

Because all animals respond differently to painful/distressful procedures and to analgesics, animals must be closely monitored during and after procedures to ensure effectiveness of analgesia.

Requirements for Analgesia

- Procedures which are expected to cause only “momentary” pain or distress (e.g., blood collection, injections) normally do not require administration of analgesic agents.
- Performance of procedures that cause pain/distress that is more than “momentary” should be accompanied by administration of an appropriate analgesic regimen that may involve both preemptive and post-procedural medications.
- With the exception of minor procedures, systemic analgesia is typically required.
- Use of a local anesthetic can be an effective component of a multi-modal analgesic regimen.
- Frequency of administration should be based upon anticipated pain response to a procedure, duration of effect of the analgesic being administered and ongoing monitoring of the animal for signs of pain. The minimum number of re-doses that will routinely be given to all animals that have the procedure should be outlined in the IACUC protocol.

Animal Pain Monitoring Considerations

- Following painful procedures, especially those that involve tissue damage, such as surgery, animals must be monitored for pain and procedural complications on a regular basis.
- Frequency of Monitoring
 - Animals must be monitored at a frequency which will allow for observation of signs of pain as the analgesic is losing efficacy and at intervals appropriate for re-dosing of analgesic drugs as indicated. Drugs may be re-dosed anytime within the drug’s time range of effectiveness.

- Example: An analgesic with expected duration of effect of 12 hours is administered at 10:00 a.m., at the start of treatment. Evaluation of the animal for pain should not be longer than 12 hours later, which is the maximum time of expected analgesic effect. The animal could be evaluated prior to 10:00 p.m. and given additional doses of analgesic if determined to be needed, or for reasons of practicality, the animal could receive a second dose of analgesic at 7:00 p.m. (9 hours following the initial dose) and then be re-assessed at 7:00 a.m. to evaluate the need for additional analgesic doses. The animal may then be monitored at 12-hour intervals until need for further analgesia has passed.
- Signs of Pain
 - Familiarity with overt signs of pain unique to each species is important to ensure that pain assessment is adequately evaluated and interpreted.
 - Rodent manifestations of pain are most commonly observed as hunched posture, lack of grooming/nest building, excessive grooming of incision sites, lethargy (lack of rearing up on hind limbs, lack of climbing on wire bars), and decreased food or water consumption. Keep in mind that rodents are prey species and tend to hide signs of pain or distress.
 - Animals that show any indications of pain must be examined to determine if additional analgesia, or other treatment, is needed.
 - If an animal showing signs of pain is treated with analgesia as described on the protocol but signs of pain persist, a veterinarian must be notified to assess the animal.

Dose Calculation and Dilution

- The importance of accurately weighing every animal in order to accurately calculate individualized doses of analgesics cannot be over-emphasized
 - Example: The difference in accurate dosing between a 20-gram and a 30-gram mouse can equate to complications ranging from inadequate analgesia to analgesic overdose.
 - When dosing multiple animals with slightly different weights, having a chart prepared in advance listing weights in small increments and associated calculated doses and injection volumes for each agent to be administered can help facilitate dosing accuracy and safety for the animal.
 - Diluting doses
 - Many drugs used in rodents are not formulated for easy use in very small animals. Many drugs have to be diluted in order to administer accurate doses in rodent species. When calculating dilutions, it is important to consider the total volume that will be administered to the animal. Volumes less than 0.1 ml (100 μ l) are often too small for dosing accurately, and volumes greater than 0.5 ml (500 μ l) may be excessive for the size of the animal and/or route of administration. Further, diluting drugs will also dilute the preservatives in injectable medications, thereby shortening the safe shelf life of the diluted drug.

Documentation

- Each administration of analgesia must be documented, either in the animal's individual Clinical Health Record, or, for rodents and non-mammals, on a group record.
 - The IACUC website provides general templates for Anesthesia/Surgery and Post-Procedural Monitoring, which may be used.
- The documentation should include an assessment of whether the animal is demonstrating any signs of pain.
 - If an animal is showing signs of pain, the record must also document how the pain was addressed.