SEDATION AND ANALGESIA IN BIRDS

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Sedation of dogs and cats in veterinary practice is daily routine for a variety of procedures, such as radiographs and ultrasonography, or other non-painful but potentially stressful procedures. However, historically for avian patients, either manual restraint of conscious birds or general anesthesia is typically performed in order to complete most clinical procedures. General anesthesia predisposes birds to cardiovascular and respiratory depression, and may cause aspiration of gastric or crop contents and hypothermia. In contrast, manual restraint in conscious birds is simple to perform, but can have negative consequences. These can include stress to the bird and/or handler, negative conditioning to the clinic environment (e.g., the person restraining or the towel used for restraint), hyperthermia, and the predisposition of trauma to the handler and/or bird. Several recent studies demonstrated that manual restraint of birds causes increased body temperature and respiratory rate.[1] In sick, old, or very stressed bird, acute collapse and death secondary to manually restraint have been reported. Therefore, sedation techniques provide a useful alternative for reducing physiologic stress in birds undergoing non-painful clinical procedures. Further, sedation in birds provides easier restraint and increases the safety of many clinical procedures (e.g. blood collection, radiography, ultrasonography) and allows for a more complete examination, which would otherwise only be achieved under general anesthesia. Using safe and effective sedative protocols in pet birds provides substantial benefits to the patients as well as the veterinarian and staff, and should be considered for a variety of clinical procedures.

Route of Drug Administration

Historically sedative drugs have been most commonly administered by intramuscular injection in birds. Recently the intranasal administration of sedative drugs in birds has gained increased attention. Intranasal administration of midazolam in Hispaniolan Amazon parrots, ring-necked parakeets, budgerigars and canary finches resulted in rapid onset of dose-dependent degree sedation, which is completely reversible with intranasal flumazenil.[1-4] Intranasal drug administration offers an alternative, non-invasive technique for drug administration in birds (Table 1). It is characterized by its ease of administration, high

bioavailability, rapid onset of action, and reduced pain compared to intramuscular administration. Elevation of muscle enzymes in biochemistry panels secondary to intramuscular drug administration is avoided, if intranasal administration is used instead. In addition, clients perceive the intranasal route as non-invasive, compared to intramuscular injection, which leads to better client compliance in cases in which sedation is recommended. The time of onset to sedation is rapid, typically within 3 - 5 minutes.[1-4] However, limitations of intranasal administration can include incomplete drug delivery, due to sneezing during administration, physiologically narrowed nostrils (e.g. cockatoos) or upper respiratory disease (e.g. blocked or stenotic nostrils). In some cases, in larger birds (e.g. macaws) the drug volume can also be limiting the effectiveness and can produce excessive sneezing, therefore leading to incomplete drug delivery. More highly concentrated drugs (e.g. midazolam 50 mg/ml, Zoopharm, Windsor, CO) are available, but intramuscular administration might be more feasible in these cases.

	Intramuscular administration	**Intranasal administration**
Pro	• Reliable drug delivery • Faster administration	• Non-invasive & not painful • Higher client acceptance • Reduced risk of needles stick injury • No changes in the biochemical panel
Con	• Invasive • Potentially painful • Possible post-injection hemorrhage • Changes in the biochemical panel	• Risk of incomplete drug delivery • Difficult to administer larger volumes • May cause sneezing • More difficult in birds with feathered nares

Table 1: Comparison of intramuscular and intranasal drug administration in pet birds

Drugs used for sedation

Midazolam is currently the most commonly used drug for sedation of pet birds and has a wide margin of safety. Midazolam has sedative, muscle relaxing, anxiolytic, amnestic and appetite stimulating properties in birds.[1,5,6] The injectable form of midazolam (midazolam hydrochloride (5 mg/ml); Hospira Inc, Lake

Forest, IL) or a more concentrated form (50 mg/ml, Zoopharm, Windsor, CO) can be administered intranasally and intramuscular, without side effects.[1-3] Dosages commonly used in pet birds range from 0.5 - 3 mg/kg.[7] At the University of Wisconsin, we routinely use 2 mg/kg of midazolam in pet birds, if administered intranasally and as the sole sedative agent. In smaller birds such as finches or budgerigars we routinely use 4-6 mg/kg of midazolam if administered alone.

Diazepam is of similar efficacy as midazolam in birds following intranasal administration, but has a longer onset time and duration of action.[3,4] While less commonly used for intranasal administration in birds, diazepam represents a suitable alternative, in cases in which midazolam might not be available. The intramuscular administration of diazepam should be avoided, due to delayed absorption and muscle irritation.[5] Dosages commonly used in pet birds range from 0.2 - 2 mg/kg, if used as a sole sedative agent. Dosages as high as 10-15 mg/kg have been administered to finches and budgerigars, without significant side effects.[3,4]

Butorphanol is the currently the most commonly used opioid analgesic in birds. Besides its analgesic effects, butorphanol has sedative effects, which are potentiated by benzodiazepines (i.e. midazolam, diazepam). The combined administration of midazolam and butorphanol is recommended in birds for which midazolam alone provides an insufficient level of sedation, or which require deeper sedation for certain clinical procedures such as radiographic positioning. Butorphanol can be given in combination with midazolam, drawn into a single syringe and can be given parenterally as well as intranasally. No side effects of intranasal administration of butorphanol at a dose range of 1 - 3 mg/kg are seen in psittacine birds.[7] _ENREF_5At the University of Wisconsin we routinely use butorphanol 1 - 2 mg/kg combined with 2 mg/kg of midazolam in pet birds administered intranasally or by intramuscular injection.

Reversal of sedation

Reversal of sedation in pet birds will depend on the patient and the purpose of sedation. Sedation performed in order to facilitate physical examination and diagnostic sample collection should always be reversed, in order to have the patient return to normal behavior and food intake as soon as possible. It is important not to discharge sedated patients, as owners do not tend to appreciate having a partially sedated bird, which might be imbalanced, sleepy and refuse to eat.

Birds that underwent sedation for e-collar or bandage placement, or that were sedated for control of seizures, should not be reversed. In these cases, birds should be carefully monitored and reversal

considered if the level of sedation is perceived too deep, or the duration of sedation is prolonged and might interfere with physiological behavior, particularly food intake.

Flumazenil is a benzodiazepine antagonist, and is used to reverse the sedative effects of midazolam and diazepam in birds.[1,2,7] The injectable form of flumazenil (flumazenil hydrochloride (0.1 mg/ml), Abaxis Pharmaceutical Products, Schaumburg, IL) can be administered intranasally, intramuscularly or intravenously, without side effects. The recommended dosages range from 0.01 - 0.1 mg/kg. Alternatively, a flumazenil to midazolam ratio of 13:1 has been recommended, but it has been shown that lower doses of flumazenil achieve complete recovery from midazolam induced sedation in birds.[1] The author prefers to administer 0.05 mg/kg initially. If reversal is deemed unsatisfactory, then the same amount of flumazenil can be administered repeatedly. Recovery from sedation is usually complete within 10-15 minutes. Reversal with flumazenil is recommended in all birds which are intended to be discharged from the hospital soon after, in order to avoid injuries from falling of perches and to avoid negative client perception of having an abnormally-behaving bird. Therefore, it is important to ensure that complete reversal has occurred prior to discharge from the hospital, by assessing complete recovery of the sensory and motor function (e.g. approaching the bird, rotating finger/perch).

Step-by-step procedure

1. Educate the bird owner about what to expect in regards to sedation of their bird. Sedation with benzodiazepines and butorphanol at the published dosages is safe in pet birds, but birds will appear sleepy, which owners are not used to. Inform them that in some cases regurgitation might occur, particularly in macaws.
2. Manually restrain the bird using a towel and immobilize the head.
3. Administer the sedative drugs into the nostrils over 5 - 10 seconds. Split the total dose between both nostrils. If intramuscular administration is performed, administer the sedative drugs by injection in the pectoral muscle using a 25 - 28 G needle.
4. Release the bird from manual restraint and allow 7 - 10 minutes for reaching maximum effect of sedation. Do not allow the bird to perch high; instead, place it on the floor or in its carrier.
5. Manually restrain the sedated bird. Monitor respiration throughout the restraint period, as well as heart rate. Perform necessary clinical procedures (e.g. physical examination, blood collection, radiographs).

6. If reversal is indicated, administer flumazenil intranasally. Split total volume between nostrils. Alternatively, flumazenil can be administered by intramuscular or intravenous injection.
7. Release the bird on the floor or in its carrier and monitor recovery. Do not allow perching high, in order to avoid trauma from falling, until the bird has completely recovered. Most birds will recover within 10-15 minutes. Assess recovery before discharging the bird. Administer a second dose of flumazenil is recovery is incomplete.

Useful tips for sedation of birds

1. Each bird requires an individual assessment prior to choosing a suitable sedative drug protocol. Birds which have no previous experiences with manual restraint may require less sedation compared to birds which had previous negative experiences and become readily stressed or fearful in a veterinary clinic environment.
2. Macaws usually require a combination of midazolam and butorphanol in order to achieve a sufficiently deep level of sedation, suitable to perform a variety of clinical procedures.
3. Even though a bird might not appear sufficiently deeply sedated while under manual restraint for a clinical procedure, it might become more sedated once stimulation is discontinued, making it unsuitable to be discharged from the hospital. Therefore, every bird which is intended to be discharged shortly after completion of the procedures performed under sedation should receive flumazenil.
4. Cockatoos often do not recover completely after the initial dose of flumazenil. A second dose of flumazenil is often necessary.

Analgesia

Significant interspecies variation in the analgesic efficacy and safety of various analgesic drugs in birds exist. Butorphanol has been historically the most commonly used opioid analgesic used in birds. Butorphanol is short acting (2-3 hours) and commonly used at 1-3 mg/kg IM. Amazon parrots should receive 3 mg/kg of butorphanol. In American kestrels butorphanol does not seem to have analgesic effects at 1-6 mg/kg. Fentanyl has been shown to reduce isoflurane MAC in red-tailed hawks at 0.2-0.5 mcg/kg/min IV; as a constant rate infusion (CRI) it may be a good intraoperative choice to provide analgesia. In cockatoos 0.2 mg/kg SC provided analgesia but also hyperactivity for 15-30 minutes. Hydromorphone in American kestrels has been shown to provide analgesia for up to 6 hours at a dose of 0.1-0.6 mg/kg IM. At the high end of the dose range sedation can occur. Tramadol is increasingly used in

avian pain management. In Hispaniolan Amazon parrots 30 mg/kg PO q6h are recommended[8], while in American kestrels 5 mg/kg PO may be sufficient to provide analgesia.[9] Raptors are more likely to become sedated if higher doses of tramadol are used.[8]

Nonsteroidal anti-inflammatory drugs (NSAIDS) are commonly used in birds. Meloxicam is the most widely used NSAID and recent research has been shown that even at high doses no clinical significant side effects occur. In Hispaniolan Amazon parrots, administration of 1.6 mg/kg PO q12h for 15 days resulted in no significant side effects.[10] The author routinely uses 1mg/kg q12-24h in pet birds. Ensure normal hydration prior to administration of any NSAID.

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