CHAPTER 77

# The Use of Butorphanol in Anesthesia Protocols for Zoo and Wild Mammals

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Butorphanol tartrate is a synthetically derived opioid agonist-antagonist analgesic of the phenanthrene series, with a potency of about four to seven times that of morphine. In the United States, it is a U.S. Drug Enforcement Administration (DEA) class IV controlled substance. Butorphanol is a mixed agonist-antagonist with low intrinsic antagonist activity at receptors of the $mu_1$ ($\mu_1$) and $mu_2$ ($\mu_2$) opioid type (morphine-like), which are responsible for the significant opioid side effects and also an agonist with a high affinity for kappa ($\kappa$) opioid receptors. Butorphanol is also a sigma ($\sigma$) receptor agonist, which stimulates respiratory drive. Its interactions with these receptors in the central nervous system apparently mediate most of its pharmacologic effects, including analgesia. Generally, there is minimal cardiopulmonary depression with its use compared with other opioids and, at lower doses, there is a dose-dependent effect on respiratory depression but then a ceiling is reached and no further respiratory depression occurs. However, there is species variability, such as a fairly marked respiratory depression when used in primates.

In veterinary medicine, butorphanol tartrate is widely used as a sedative and analgesic in dogs, cats, and horses. It is administered either IM or IV, with its analgesic properties beginning to take effect about 15 minutes after IM injection and lasting about 4 hours. The elimination half-life is about 18 hours. For increased sedation or light anesthesia, it may be combined with sedatives such as $\alpha$-adrenergic agonists (e.g., medetomidine, xylazine) or tranquilizers such as benzodiazepines (e.g., midazolam, diazepam) or phenothiazines (e.g., acepromazine) in dogs and cats. In horses, butorphanol is frequently combined with sedatives (e.g., xylazine, detomidine, romifidine) to make the horse easier to handle during veterinary procedures.

Butorphanol is relatively safe, with a high therapeutic index, and may be completely reversed rapidly with naloxone, nalmefene, or naltrexone, or partially reversed by diprenorphine, which antagonizes only the $\mu$ opioid receptors but not the $\kappa$ opioid receptors. This partial reversal of the undesirable $\mu$ opioid receptor effects (muscle tremors, tachycardia-bradycardia, gastrointestinal stasis, euphoria-dysphoria, respiratory depression) while maintaining the sedative $\kappa$ effect produces some useful and safer anesthetic protocols in nondomestic species.

As with other opioid analgesics, central nervous system effects (e.g., sedation, excitement) are considerations with the use of butorphanol. Nausea and vomiting are common. Less common are the gastrointestinal effects of other opioids, mostly constipation. Butorphanol is transported across the blood-brain and placental barriers and into milk. It is extensively metabolized in the liver with urinary excretion.

In zoo and wildlife species (mainly mammal), it is being used for one or more of the following: (1) pain control; (2) combined with sedatives to assist in minor manipulative procedures; (3) combined with $\alpha_2$-adrenergic agonists and/or more potent opioids for anesthesia or neuroleptanalgesia. Butorphanol, when used alone, causes apathetic sedation that may allow arousal when the animal is stimulated, a potential danger when working with dangerous species.

Butorphanol combined with $\alpha_2$-adrenergic agonists, potent opioids, dissociative anesthetics and/or tranquilizers may produce safer anesthesia procedures by minimizing many adverse effects. These combinations use lower doses of each agent and use the synergistic effects of the various drugs in the combination.

Butorphanol appears to be the opioid analgesic of choice for birds because analgesia is primarily regulated thorough $\kappa$ receptors in birds; however, its analgesic efficacy is limited because of its short half-life in birds.[25] The development of a liposome-encapsulated

formulation of butorphanol tartrate has extended its analgesic efficacy in birds to 3 to 5 days. Butorphanol has shown promise as a premedication for some avian species undergoing isoflurane inhalation anesthesia (see Chapter 41).

Butorphanol use in reptiles has shown limited analgesic effect and minor effects have also been seen when it is incorporated into various anesthetic protocols.[24,26] Because analgesia, in most reptiles studied to date, is μ opioid receptor–dependent, drugs such as morphine work best for analgesia.

The initial low commercial concentrations of butorphanol (10 mg/mL) made larger dart volumes necessary, which in turn adversely affected the performance and range of the dart. The various anesthetic protocols that use butorphanol are becoming more popular with the development of more concentrated formulations (30 and 50 mg/mL) that allow its use in remote delivery systems. One such formulation, containing butorphanol, azaperone, and medetomidine (BAM), has proved successful in a wide range of species.

Butorphanol combinations with tranquilizers and/or an $\alpha_2$ agonist at low dosages are used together with restraint devices for standing restraint procedures in captive elephants, rhinoceros, giraffes, and tapirs.

## USE IN VARIOUS SPECIES

### Captive Elephant

As with other species, drug dosages for the sedation and anesthesia of elephants often vary among species and among individuals, so extrapolations should be used with caution. Butorphanol has been used mainly in combination with azaperone or $\alpha_2$-adrenergic agonists (e.g., detomidine, xylazine) to manage excitable animals and/or for minor manipulative procedures.

In one report involving 14 standing clinical procedures in African elephants *(Loxodonta africana)*, a recommended starting dosage range of 14.7 to 16.2 μg/kg of both detomidine and butorphanol in a ratio of 1 : 1, on a microgram to microgram basis, were administered simultaneously IM. The initial effect was noted within 3.0 to 25 minutes (mean, 11.6 minutes; standard deviation [SD], ±5.9 minutes), with maximal effect occurring at 25 to 30 minutes for those procedures not requiring supplementation. This could subsequently be supplemented as needed using 4.0 to 7.3 μg/kg of each drug. Recovery after administration of reversal agents was rapid and complete, ranging from 2 to 20 minutes (mean, 9.0 minutes; SD, ±7.0 minutes).[18]

In Asian elephants *(Elephas maximus)*, a dose of 0.01 to 0.03 mg/kg administered IV, IM, or SC is suggested for minor manipulative procedures.[10] For aggressive adult African elephants, xylazine, 700 to 1000 mg/adult elephant (≈0.2 to 0. 3 mg/kg), followed by IV butorphanol, 50 to 180 mg/adult elephant (≈0.01 to 0.03 mg/kg), has proven effective.[22]

A xylazine-butorphanol combination was successfully used for standing restraint of Asian elephants at average doses of xylazine (70 μg/kg) and butorphanol (25 μg/kg) IV and reversal with naltrexone at approximately 50 μg/kg and yohimbine at 0.1 mg/kg. Atipamezole administered at 4 μg/kg IV provided better xylazine reversal than yohimbine.

### Captive Rhinoceros

Butorphanol alone and in combinations with other tranquilizers and/or $\alpha_2$-adrenergic agonists may facilitate many management and medical procedures, with or without restraint devices.

The use of a medetomidine-butorphanol combination for standing and recumbent chemical restraint of the white rhinoceros *(Ceratotherium simum)* has produced good results.[21] A mean dose of 63 ± 1.2 μg/kg butorphanol plus 2.64 ± 0.17 μg/kg medetomidine is given IM. Average doses for adult white rhinos are medetomidine, 5 to 7 mg, and butorphanol, 80 to 150 mg. Midazolam may be added to this cocktail at a total dose of 20 to 40 mg to improve relaxation. Animals become safe to work on in a standing position in about 8 to 20 minutes and then may be pulled down into recumbency, or supplemented with ketamine, 200 to 400 mg IV, to induce recumbency. Supplemental drugs used to maintain chemical restraint for long procedures include a constant rate IV infusion using guaifenesin 5% in dextrose, ketamine, butorphanol, medetomidine, propofol, or a combination of these. A wide range of procedures has been accomplished using these combinations, including electroejaculation, fiberoptic endoscopy, ophthalmic surgery, dental procedures, and daily repeated IV therapy. Reversal is accomplished with naltrexone, 233 ± 29 μg/kg (one to two times the butorphanol dose) and atipamezole, 14.7 ± 3.8 μg/kg (five times the medetomidine dose).[6]

Butorphanol is useful for modulating opioid receptor effects when etorphine is used in rhinoceroses. If etorphine combinations are used, partial reversal with butorphanol (titrate with 10 mg IV boluses) will reduce respiratory depression without getting arousal in the white rhinoceros.

For crate loading white rhinoceroses, a combination of etorphine-butorphanol-midazolam is useful. Doses are etorphine, 0.5 to 0.7 µg/kg, butorphanol, 15 to 25 µg/kg, and midazolam 15 to 25 µg/kg (average total doses for adults—etorphine 1.0 mg, butorphanol, 30 mg, midazolam, 30 mg). Etorphine causes the animal to continue to walk forward for loading. Once in the crate and loaded on the truck, the etorphine is reversed with diprenorphine at twice the etorphine dose; this only reverses the etorphine and leaves the butorphanol and midazolam on board for travel. Animals should be observed during travel for excessive pressing or getting into dangerous positions. If animals need to be fully reversed, they may be given naltrexone at one to two times the butorphanol dose. If various butorphanol combinations without etorphine are used for loading white rhinoceroses, the animals will tend to just stand and not move forward, so they may be difficult to load.

Two butorphanol combinations have been used in the captive black rhinoceros *(Diceros bicornis)*—butorphanol-azaperone and butorphanol-detomidine—but they are not recommend because restraint is not as good as with the white rhinoceros, which could be very dangerous for less experienced people. The black rhinoceros does not experience as much respiratory depression and other physiologic disturbances with etorphine as the white rhinoceros, so butorphanol combinations are generally not necessary.

Standing procedures on the Asian greater one-horned rhinoceros *(Rhinoceros unicornis)* using medetomidine-butorphanol-midazolam has been used successfully; average doses are medetomidine, 3 to 4 µg/kg, butorphanol, 50 to 60 µg/kg, and midazolam, 12 to 15 µg/kg. Most of these procedures have been for reproductive examinations on females (rectal ultrasound) and for IV therapy in sick rhinoceroses. Supplemental ketamine (200 to 400 mg IV) will produce recumbency. Reversal is with naltrexone at twice the butorphanol dose and atipamezole at five times the medetomidine dose. Standing sedation has also been produced in the Indian rhinoceros *(R. unicornis)* using a butorphanol-azaperone combination (adult, 100 mg of each).[20]

As with white rhinoceroses, butorphanol combinations are preferred in Sumatran rhinoceroses *(Dicerorhinus sumatrensis)* because better muscle relaxation and improved cardiopulmonary function are obtained when compared with the more potent opioids. A butorphanol (30 to 50 mg) and azaperone (50 to 60 mg) combination in adults may be used for standing sedation at the lower end of the dosage range or recumbency at the higher dosages.[20] A second combination using medetomidine (2.0 to 2.5 µg/kg) and butorphanol (70 to 72 µg/kg) produces a good standing chemical restraint in Sumatran rhinoceroses, after which they may be pulled into sternal recumbency. This combination also maintains acceptable physiology. Reversal is with naltrexone at twice the butorphanol dose and atipamezole at five times the medetomidine dose.

## Captive Giraffe

The physical restraint of giraffe *(Giraffa camelopardalis)* in a confinement chute may be enhanced by the use of sedatives and tranquilizers. The combination of azaperone (250 to 350 µg/kg) plus detomidine (15 to 30 µg/kg) given IM produces good tranquilization and moderate analgesia. This combination facilitates blood sampling, reproductive examinations, tuberculin testing, joint taps, radiographs, suturing, and dystocia corrections. To increase sedation, 10 mg of butorphanol IV is used in adult animals. The detomidine is partially reversed with yohimbine (0.1 mg/kg) or atipamezole (0.2 mg/kg) and the butorphanol is reversed with naltrexone (2 mg naltrexone/1 mg butorphanol).

## Captive Okapi

For standing chemical restraint in okapi *(Okapia johnstoni)*, combinations of either xylazine (0.4 to 0.8 mg/kg) and butorphanol (80 to 200 µg/kg) or detomidine (40 to 100 µg/kg) and butorphanol (80 to 200 µg/kg) provides good standing restraint for a variety of clinical procedures, including venipuncture, IV catheter placement, hoof trimming, endoscopy, bronchoalveolar lavage, insemination, rectal and transcutaneous ultrasound, thoracocentesis, and minor surgery. Animals will move around a bit, but otherwise the sedation is satisfactory. Reversal for the $\alpha_2$-adrenergic agonist is with yohimbine, 0.1 to 0.2 mg/kg, or tolazoline, 0.5 mg/kg, and/or atipamezole, 30 to 50 µg/kg. The butorphanol is reversed with naltrexone at one to two times the butorphanol dose, if desired.

## Other Ruminants

To improve analgesia and prolong down time in the gerenuk *(Litocranius walleri)* and other small ruminants anesthetized with medetomidine (60 to 70 µg/kg) and ketamine (2 to 3 mg/kg), butorphanol can be added to the anesthetic regimen. This has been very useful for electroejaculation in this species. Reversal is with

atipamezole at five times the medetomidine dose and naltrexone at twice the butorphanol dose.

Medetomidine-butorphanol-ketamine has also been studied in Thomson's gazelles *(Gazella thomsoni)* with doses of medetomidine, 40.1 ± 3.6 µg/kg, butorphanol, 0.40 ± 0.04 mg/kg, and ketamine, 4.9 ± 0.6mg/kg. This combination was successfully used for the castration of male Thompson's gazelles with the addition of local blocks at the surgical site. Mild hypoxemia and hypoventilation were seen in some animals not supplemented with intranasal oxygen. Animals stood within 12 minutes after reversal with atipamezole (0.20 ± 0.03 mg/kg) and naloxone (0.02 ± 0.001 mg/kg).[5]

The San Diego Zoo has reported excellent results using butorphanol (0.2 to 0.25 mg/kg) with medetomidine (0.03 mg/kg) for the chemical restraint of the takin *(Budorcas taxicolor)*. Side effects included bradycardia and low oxygen saturation values. Nasal insufflation with oxygen helped maintain good oxygen saturation readings. Reversal with IM naltrexone (0.35 mg/kg) and atipamezole (five times the medetomidine dose) combination typically results in a smooth recovery in 7 to 8 minutes.[17]

A mixture of tiletamine-zolazepam (1.2 mg/kg) and butorphanol (0.1 mg/kg), and an equipotent sedative dose of $\alpha_2$-adrenergic agonist (xylazine, detomidine, or medetomidine) was used in 18 different species of ungulates for routine medical procedures. To supplement the anesthesia, a 25-mg IV bolus of ketamine was given; this showed no after effect following reversal of the anesthesia with tolazoline (4 mg/kg) or atipamezole (1 mg/8 to 10 mg of xylazine) and naltrexone (1 mg/10 mg butorphanol). In some situations, the butorphanol was not reversed. Recovery times were not significantly affected by not reversing the butorphanol with naltrexone but the animals were not as alert following reversal. Rapid reversal with atipamezole was complete as expected in all combinations, with no recurrent sedation following antagonism. Despite being administered half IM and half SC, atipamezole reversed the effects more rapidly than tolazoline administered completely IV (1 to 8 minutes for atipamezole; 2 to 15 minutes for tolazoline). The zolazepam was not reversed.[19]

The San Diego Zoo uses a combination of medetomidine (70 to 100 µg/kg), butorphanol (300 µg/kg), and midazolam (300 µg/kg) for chemical restraint of its wild swine species and reversal with atipamezole (80 to 100 µg/kg) and naltrexone (350 to 700 µg/kg). If flumazenil is required to reverse midazolam; it is used at a ratio of 1 : 10 to 1 : 20 the dose of midazolam.[16]

A detomidine (59 to 79 µg/kg)-butorphanol (50 to 88 µg/kg) combination has been used for standing sedation in the banteng *(Bos javanicus)*. For recumbent anesthesia, a combination of detomidine (69 to 104 µg/kg), butorphanol (71 to 83 µg/kg), and ketamine (0.60 to 2.78 mg/kg) has been used, with reversal with naltrexone and yohimbine.[7]

## Tapir

In Baird's tapirs *(Tapirus bairdii)*, a combination of medetomidine (6 to 8 µg/kg) and butorphanol (0.16 to 0.20 mg/kg) produces a good anesthesia. The combination can be reversed with atipamezole at five times the medetomidine dose and naltrexone at twice the butorphanol dose.[27]

Twenty immobilizations of 16 free-ranging Baird's tapirs in Corcovado National Park, Costa Rica, were successfully performed with a butorphanol-xylazine combination administered by remote injection. Tapirs were estimated to weigh between 200 and 300 kg. Butorphanol (48 ± 1.84 mg/animal) and xylazine (101 ± 2.72 mg/animal) were used. In some cases, ketamine was used IM or IV at 187 ± 40.86 mg/animal to prolong the anesthesia period. Naltrexone (257 ± 16.19 mg/animal) IM was used to reverse butorphanol. Yohimbine (34 ± 0.61 mg/animal) or tolazoline (12 ± 10.27 mg/animal) was used to reverse xylazine.[9]

A male Malayan tapir (*Tapirus indicus*; estimated weight of 340 kg) with oral squamous cell carcinoma was successfully treated under anesthesia using IM butorphanol (80 mg [0.24 mg/kg]) and either xylazine (120 mg [0.35mg/kg]) or detomidine (12 mg [35 µg/kg]).[15]

## Equids

Good standing restraint in Grevy's zebra *(Equus grevyi)* may be produced using a combination of detomidine (0.1 to 0.15 mg/kg) and butorphanol (0.2 to 0.25 mg/kg). Animals may then be induced to recumbency with an IV bolus of ketamine (200 to 500 mg total dose). Reversal can be accomplished with naltrexone at twice the butorphanol dose and yohimbine at 0.1 to 0.2 mg/kg plus tolazoline at 0.25 mg/kg.

The Somali wild ass *(Equus asinus)* may be anesthetized using a combination of etorphine (3 to 3.5 mg), detomidine (10 to 12 mg), and acepromazine (5 to 6 mg), but they developed significant respiratory depression ($SpO_2$ = 70% to 80%). Butorphanol (10 mg IV) can be used for partial reversal of the µ opioid effects of

etorphine; within 5 minutes of administration, $SpO_2$ values rise to more than 90%.

For a more effective immobilization of the free-ranging Asiatic wild ass, butorphanol (10 mg) is added to the darting combination of etorphine (2.5 to 3.0 mg) and detomidine (10 mg), because butorphanol reduces respiratory depression and limits the etorphine-specific pacing, so that animals travel less distance after darting.[28]

## Carnivores

For a completely reversible anesthesia in the cheetah *(Acinonyx jubatus)*, a combination of medetomidine (35 ± 3.7 µg/kg), butorphanol (0.2 ± 0.02 mg/kg), and midazolam (0.15 ± 0.02 mg/kg) has proved successful. This combination has been used in more than 200 cheetahs, including very sick animals. Physiologic parameters remained good, except for bradycardia, accentuated sinus arrhythmia, and mild to moderate hypertension. This combination seems ideal for field procedures in which quick recovery and release are desirable. Reversal was complete with IM atipamezole at five times the medetomidine dose, naltrexone at 0.25 mg/kg, and flumazenil at 6 µg/kg.[13]

A reversible anesthetic combination using medetomidine (44.5 ± 9.1 µg/kg), butorphanol (0.24 ± 0.06 mg/kg), and midazolam (0.29 ± 0.1 mg/kg) was used successfully in a semi–free-ranging setting for the chemical restraint of African wild dogs *(Lycaon pictus)*.[8] Mean induction times were 6 ± 5 minutes and acceptable physiology was monitored during a 38-minute working time (±6 minutes). The effects on the wild dogs were reversed with IM injections of atipamezole, 3 mg, naltrexone, 10 mg, and flumazenil, 0.2 mg. A similar successful study was done on free-ranging spotted hyena in Kruger National Park, with good results.[12]

A combination of IM medetomidine (0.4 mg/kg) and butorphanol (0.4 mg/kg) was evaluated in 16 red wolves *(Canis rufus)*. Seven wolves received only medetomidine and butorphanol, and the other 9 wolves also received IV diazepam once the animal was down. Both these combinations produced a completely reversible anesthetic that also prevented the undesirable effects of hypertension and prolonged and rough recoveries; these were previously noted when an $\alpha_2$-adrenergic agonist and ketamine were used for anesthesia. The reversal used IM atipamezole (0.2 mg/kg) for the medetomidine and naloxone (0.02 mg) for the butorphanol. The diazepam was reversed with IV flumazenil (0.04 mg/kg).[14]

Veterinary Wildlife Services, South African National Parks, have recently conducted a field trial ($N = 30$) in adult and subadult lions *(Panthera leo)* using a combination of butorphanol (0.3 mg/kg), medetomidine (0.05 mg/kg), and midazolam (0.2 mg/kg) and found it to be a very effective immobilizing drug combination.[2] Induction times were rapid, the animals were very stable while immobilized, and the combination could be reversed at any time. During the trial, the effects were reversed after 45 minutes, but subsequent use of the combination has shown it to be effective for at least 1.5 hours. In the initial stages of the study, all lions were blindfolded and had their front limbs hobbled in the event of a spontaneous recovery; at these dose rates, this still could happen. The antidotes are IV naltrexone (2.2 times the butorphanol dose), atipamezole, both IV and SC (2.5 times the medetomidine dose), and IV flumazenil (0.016 times the midazolam dose). We have subsequently found that it is not essential to administer the flumazenil, especially if the animals have been immobilized for longer than 1 hour. Reversal was smooth and rapid. This combination is proving to be very effective in immobilizing lions because the effects may be completely reversed; the main drawback is the costs of the drugs.

As a safety rule, it is a good idea to use caution and have some restraint of large dangerous carnivores when medetomidine and/or butorphanol are used without a dissociative anesthetic (ketamine or tiletamine-zolazepam) in the protocol, because sudden arousal may occur, especially at lower doses of medetomidine and/or butorphanol.

## African Buffalo

The captive management of specific disease-free African buffalo *(Syncerus caffer)* is a major economic concern in Southern Africa. Presently, extensive testing is required to certify the disease status of those animals requiring repeated anesthesia and manipulation; also, there is extensive relocation of disease-free buffalo. The use of butorphanol has been shown to assist in and facilitate the management of these large, dangerous, and belligerent animals.[11] The buffalo are first anesthetized using etorphine-azaperone combinations at 8 and 12 mg total dosage, respectively, for bulls and 6 and 50 mg for cows. To move the animals to a transport vehicle or crate, the buffalo, which are blindfolded and have earplugs, are given IV butorphanol (25 mg for cows and 50 mg for bulls). After 45 seconds, the animals may be stimulated to stand and walk passively to the desired destination,

which minimizes the physical effort of carrying them. The butorphanol also improves the respiration of the buffalo and thus the safety of the procedure.

## BUTORPHANOL-CONTAINING ANESTHETIC COCKTAILS

The butorphanol combination that has rapidly come into use in hoofstock and large carnivores since 2008 is a mixture, BAM, in an approximate ratio of butorphanol (30 mg/mL), azaperone (18 mg/mL), and medetomidine (10 mg/mL). The combination concentrations and total dose volumes are adjusted slightly in some species. The total dose volumes range from 0.5 to 3 mL in most species. Table 77-1 lists various species and average doses.

This combination has been successfully used to anesthetize female white-tailed deer (65 to 75 kg) using 1.0 to 1.5 mL of the combination. Large, mature, white-tailed male deer may require up to 2.5 mL of this formulation. Over 1000 white-tailed deer have been anesthetized in Texas with this combination.[3] Large members of the family Felidae (lions, tigers, mountain lions) may be anesthetized with very small dart volumes of this combination (0.5 to 1.0 mL. In these large felids, the addition of ketamine to the protocol has resulted in a more effective anesthesia.[1] Induction to sternal recumbency usually requires 7 to 15 minutes and is extremely smooth and controlled. Anesthesia with this combination is characterized by lack of postinduction hyperthermia, excellent respiration rates and patterns, and good muscle relaxation. The anesthesia may be reversed IM with atipamezole (3 mg/mg of medetomidine) or tolazoline (100 mg for every 10 mg of medetomidine) and naltrexone (50 mg for every 30 mg of butorphanol). The reversal is rapid and complete in less than 10 minutes in most species.

This BAM combination has not produced acceptable anesthesia in fallow deer. It has been tried for anesthesia for semen collection in white-tailed deer but the results have not been acceptable.

### Rhinoceros Anesthesia

One study has compared a standard anesthesia protocol with the same protocol containing butorphanol in a capture cocktail for the capture of 31 white rhinoceroses. The control group contained 15 animals.[29] The standard anesthetic mixture used in both groups included etorphine, azaperone, and detomidine plus hyaluronidase, and dosages were adjusted for the age of the animal. In the study group, butorphanol (10 to 20 mg) was added to the anesthetic combination. No difference in induction time was noted, but the distance traveled following darting was shorter in the butorphanol group. They also reported no improvement in the measured physiologic parameters in the butorphanol group. Both groups showed metabolic acidosis, hypercapnia, and

**TABLE 77-1** Butorphanol, Azaperone, and Medetomidine (BAM) Dosages in Hoofstock and Carnivores

| | | BAM DOSAGES (MG/KG, AVERAGE) | | |
|---|---|---|---|---|
| Study (Year) | Species | Butorphanol | Azaperone | Medetomidine |
| Seigal-Willot et al (2009)[23]; Wolfe (2010)* | White-tailed deer, *Odocolieus virginianus* | 0.58 | 0.37 | 0.19 |
| Wolfe (2010)* | Mule deer, *Odocoileus hemionus* | 0.58 | 0.37 | 0.19 |
| Wolfe (2010)* | Elk, *Cervus elaphus* | 0.11 | 0.07 | 0.05 |
| Wolfe (2010)* | Pronghorn, *Antilocapra americana* | 0.74 | 0.68 | 0.28 |
| Wolfe (2010)* | Bighorn sheep, *Ovis canadensis* | 0.44 | 0.26 | 0.20 |
| Shury (2010)† | Bison, *Bison bison* | 0.29 | 0.14 | 0.07 |
| Armstrong (2010)[1]; Wolfe et al (2008)[30] | Large felids | 0.159 | 0.128 | 0.053 |
| Wolfe (2010)* | Przewalski's horse, *Equus caballus przewalskii* | 0.09 | 0.08 | 0.07 |
| Citino (2010)‡ | Nile hippopotamus, *Hippopotamus amphibibus* | 0.10 | 0.10 | 60 µg/kg |

**Wolfe L: Personal communication.*
*†Shury T: Personal communication.*
*‡Citino SB: Personal experience.*

**TABLE 77-2** Physiologic Data on Awake and Anesthetized White Rhinoceros

| Time | pH | $Po_2$ (mm Hg) | $Pco_2$ (mm Hg) | $O_2$ Saturation (%) | Base Excess (mEq/liter) | Heart Rate (beats/min) | Respiratory Rate (breaths/min) | Systolic Blood Pressure (mm Hg) |
|---|---|---|---|---|---|---|---|---|
| **Awake Rhinoceros ($n$ = 12)** | | | | | | | | |
| — | 7.391 | 98.2 | 49 | 97.2 | 3.5 | 39 | 19 | 160 |
| **Standard Protocol: Etorphine + Azaperone ($n$ = 10)** Ref 4 | | | | | | | | |
| 0 time | 7.175 | 35 | 62 | 49 | −6.4 | 139 | 10 | 190 |
| 10 min | 7.246 | 37 | 70 | 62 | −0.3 | 122 | 11 | 151 |
| 20 min | 7.244 | 41 | 64 | 69 | −1.4 | 103 | 9 | 159 |
| **Protocol 1: Etorphine + Butorphanol + Midazolam ($n$ = 48)** | | | | | | | | |
| 0 time | 7.270 | 56 | 48 | 89 | −4.7 | 74 | 9 | 141 |
| 10 min | 7.284 | 59 | 50 | 89 | −3.0 | 65 | 9 | 143 |
| 20 min | 7.305 | 59 | 51 | 90 | −1.4 | 62 | 9 | 136 |
| **Protocol 2: Protocol 1 With a Partial Reverse Using Diprenorphine M50-50 (at 12 min; $n$ = 16)** | | | | | | | | |
| 0 time | 7.289 | 46 | 52 | 82 | −0.1 | 84 | 11 | 141 |
| 10 min | 7.316 | 59 | 48 | 89 | −2.1 | 65 | 10 | 140 |
| 20 min | 7.350 | 67 | 48 | 92 | −0.3 | 59 | 11 | 137 |

hypoxemia. Their conclusion was that the addition of butorphanol had little effect on the anesthetic procedure.

We have studied the anesthetic combination of etorphine, butorphanol, and midazolam in 64 free-ranging white rhinoceroses in South Africa and our results differ from the above report.[4] As in the study noted, we observed no mortality or morbidity in the study animals. We found that the following combination provides the best results: etorphine (1.5 ± 0.5 µg/kg), butorphanol (50 ± 15 µg/kg), plus midazolam (25 ± 5 µg/kg).

The data from captive awake white rhinoceroses has served as a baseline for evaluation of the effect of our anesthetic protocols (Table 77-2).[4] We compared these normal parameters with a previous standard protocol (etorphine-azaperone combination) used in white rhinoceroses. Note in this table the marked hypoxemia, elevated $Pco_2$, slight acidosis, and elevated heart rate observed when the standard protocol is used. We currently believe that the addition of butorphanol to the anesthetic combinations at the ratio of at least 20:1 butorphanol to etorphine for white rhinoceros anesthesia greatly improves the physiologic status and safety of the animal during the procedure compared with previous anesthetic protocols such as the etorphine-azaperone combination. This was indicated by improved hemoglobin oxygen saturation, decreased heart rate, and improved muscle relaxation, which in turn improves respiratory efficiency.

With this combination, an initial slightly higher dose of etorphine than usually used may be required to produce recumbency. It should be noted that although the down time is longer, the rhinoceroses tend to stop walking within 5 to 6 minutes. We also found it helpful to let the animals stand longer (5 minutes) before manipulation because this results in a smoother anesthesia. This combination offers another unique safety factor in the case of respiratory depression, The administration of a low IV dose of diprenorphine (M 50-50) (1 mg) will further antagonize the µ opioid effect of etorphine that caused the depressed respiration, muscle rigidity and tremors, and tachycardia, thus improving the physiologic parameters (see Table 77-1). Sedation and control of the animal are maintained by the κ opioid receptor sedation of the butorphanol and the tranquilizer midazolam. With this partial reversal of the anesthesia, the animal may be induced to stand and walked into a crate for transportation. Once loaded, the animal rides very well, with less head pressing because of the reversal of the µ opioid effect; sedation is maintained by the κ opioid effect of the butorphanol combined with midazolam. To reverse the etorphine and butorphanol, naltrexone is used because it reverses both µ and κ opioid effects, allowing the animal to regain its feet with only mild sedation remaining due to midazolam.

The differences reported in the results and conclusions from these two reports are probably the result of the use of both azaperone and detomidine with the etorphine, whereas we used only midazolam. Also, our ratio of butorphanol to etorphine was higher, at least 20:1 butorphanol to etorphine; they used a ratio of about 10:1 or lower.[29]

## Drugs Mentioned in the Text

Atipamezole (Antisedan)—Farmos Pharmaceuticals; Turku, Finland
Azaperone (Stresnil)—Wildlife Pharmaceutical, Inc; Fort Collins, Colorado
Butorphanol (Butorphanol)—Wildlife Pharmaceutical, Inc; Fort Collins, Colorado
Etorphine (M99)—Wildlife Pharmaceutical, Inc; Fort Collins, Colorado
Flumazenil (Romazicon)—Roche Laboratories, Inc.; Nutley, New Jersey
Ketamine (Ketaset)—Fort Dodge Animal Health, Fort Dodge, Iowa
Naltrexone (Trexonil)—Wildlife Pharmaceutical, Inc; Fort Collins, Colorado
Medetomidine (Medetomidine)—Wildlife Pharmaceutical, Inc; Fort Collins, Colorado
Xylazine (Rompun)—Bayer Corporation; Shawnee, Kansas
Tiletamine–zolazepam (Telazol)—Fort Dodge Laboratories; Fort Dodge, Iowa
Tolozoline (Tolazine)—Lloyd Incorporated; Shenandoah, Iowa
Yohimbine (Antagonil)—Wildlife Pharmaceutical, Inc; Fort Collins, Colorado

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