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CHEMICAL IMMOBILIZATION OF FREE-RANGING WHITE RHINOCEROS (*CERATOTHERIUM SIMUM SIMUM*) IN HWANGE AND MATOBO NATIONAL PARKS, ZIMBABWE, USING COMBINATIONS OF ETORPHINE (M99), FENTANYL, XYLAZINE, AND DETOMIDINE

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Abstract: One hundred forty-one free-ranging white rhinoceros (*Ceratotherium simum simum*) of various ages were immobilized in 1991 ($n = 71$) and 1992 ($n = 70$), and the majority were dehorned as part of a conservation program to prevent poaching. Twenty-three animals were darted by personnel on foot and 118 were darted from a helicopter. Fifty-six adult animals were immobilized using a mean (±SEM) dose per animal of 4.2 ± 0.11 mg etorphine combined with 123 ± 4.7 mg xylazine, 13 adult animals were immobilized using a mean dose of 2.03 + 0.06 mg etorphine and 29.2 ± 0.8 mg fentanyl, 60 adult animals were immobilized with a mean dose of 3.9 + 0.15 mg etorphine and 13.1 ± 0.43 mg detomidine, and 12 animals (subadults and calves) were immobilized with a mean dose of 1.16 + 0.28 mg etorphine alone. Hyaluronidase (1,500 IU) was mixed with all drug combinations. The mean induction time for all combinations was 6.4 ± 0.37 min (median = 5 min), with no significant differences in induction times among animals injected with the various drug combinations. The mean duration of immobilization was 38 ± 1.7 min. In 1991, mean reversal time following the administration of naloxone (i.v., 64 ± 4 mg, $n = 56$) and diprenorphine (i.m., 12.4 + 0.7 mg, $n = 54$) was 93 ± 7 sec, and when naltrexone became available in 1992, mean reversal time was 92 + 5 sec (i.v., 70 + 2 mg, $n = 68$). The etorphine/detomidine combination produced significantly less muscle damage, based on creatine phosphokinase (IU/L) measurements, than did the other drug combinations. Serum cortisol (μg/dl) values for subadults and calves immobilized were significantly higher than those in adults, indicating increased stress. Pulse rates for those animals immobilized with etorphine/detomidine were significantly lower than those of animals immobilized with the other drug combinations. Prolonged recumbency was associated with hypoxemia, pulse oximetry revealed a saturated blood oxygen (Sao_2) of 40–60% in recumbent rhinoceros, which was improved by ≥ 20% using 10–20 mg nalorphine or 20–40 mg nalbuphine, administered i.v. Of the 71 animals immobilized in 1991, five animals died (mortality rate = 7%); three of these deaths were most likely associated with hypoxemia and cardiovascular system collapse. There were no direct capture-related mortalities recorded in the immobilization of 70 animals in 1992 (overall mortality rate for 1991/1992 = 3.4%).

Key words: White rhinoceros, *Ceratotherium simum*, immobilization, etorphine, fentanyl, xylazine, detomidine, diprenorphine, naloxone, naltrexone, nalorphine, nalbuphine, pulse oximetry.

INTRODUCTION

Over 140 white rhinoceros (*Ceratotherium simum simum*) have been chemically immobilized during dehorning operations in Zimbabwe in 1991 and 1992 as part of a conservation strategy for both black and white rhinoceros.[16,18,27] There are few recent published reports concerning chemical immobilization of the white rhinoceros, both free ranging and captive.[2,4,11,23] In 1993, significant capture and management recommendations for this species were published.[21] However, few reports since the 1960s have critically evaluated the drugs used,[3,7–10,14,15,20,22,25] and established mixtures have not changed for decades.[21] The dehorning operations in Zimbabwe have allowed the critical evaluation of several drug

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combinations used for chemical immobilization. In this report, we evaluate etorphine alone and in combination with fentanyl, xylazine, or detomidine with regard to induction times, quality of anesthesia, and the effects of various drug combinations on physiological and biochemical measurements indicative of stress. A mixed agonist–antagonist opioid and a long-acting pure opioid anatagonist were also evaluated.

MATERIALS AND METHODS

White rhinoceros of various ages were immobilized in Hwange National Park (NP) (n = 110), located in North-West Matabeleland (19°S, 26.5°E), and Matobo NP (n = 31) (20.5°S, 28.5°E) located south of the city of Bulawayo.

Animals were darted in the early morning or the late afternoon, depending on the weather conditions and ambient temperature. Animals were located using a combination of ground tracking, fixed-wing aircraft, and helicopter. Twenty-three animals were darted by personnel on foot, and 118 were darted from a helicopter.

All animals were darted with a mixture of etorphine (M99, 9.8 or 4.8 mg/ml, C-Vet Ltd., Bury St. Edmunds, U.K.) and fentanyl (Sublimaze, 40 mg/ml, Ethnor Ltd., Halfway House, Republic of South Africa), etorphine and xylazine (Rompun, 100 mg/ml, Bayer, Leverkusen, Germany), or etorphine and detomidine (Domesedan, 10 mg/ml, Ciba Geigy Ltd., Steel Road, Spartan 1620, South Africa) or with etorphine alone. Hyaluronidase (Hyalase, 1,500 IU/vial, Dougal Morton, University of Zimbabwe, P.O. Box MP 167, Harare, Zimbabwe) was mixed with all drug combinations. Immobilization was reversed either with a combination of naloxone (i.v.) (50 mg/ml, Wildlife Laboratories, Fort Collins, Colorado 80525, USA) and diprenorphine (i.m.) (M50-50, 12 mg/ml, C-Vet Ltd.) or with naltrexone (i.v.) (50 mg/ml, Wildlife Laboratories). Fifty-six animals (all adults) were immobilized using a combination of etorphine (4.2 ± 0.11 mg) and xylazine (123 ± 4.7 mg), 13 animals (all adults) were immobilized with etorphine (2.03 ± 0.06 mg) and fentanyl (29.2 ± 0.8 mg), 60 animals (all adults) were immobilized with etorphine (3.9 ± 0.15 mg) and detomidine (13.1 ± 0.43 mg), and 12 animals (calves <3 yr old) were immobilized with etorphine alone (1.16 ± 0.28 mg). To counteract postinduction respiratory depression, several drugs were utilized, including nalorphine hydrobromide (Nalorphine, 20 mg/ml, Kyron Laboratories, Benrose 2094, South Africa), nalbuphine hydrochloride (Nubain, 10 mg/ml, Boots Co., Isando, South Africa), and dopram hydrochloride (Doxapram, 20 mg/ml, Continental Ethicals, Port Elizabeth, South Africa).

Projectile syringes were 3–4 ml in volume with 47–68-mm collared needles. Both bevelled and nonbevelled needles were used (D. L. Tranquillizer Systems, Fenny Bentley, Derbyshire, U.K., and CapChur, Palmer Chemical and Capture Co., Douglasville, Georgia 30134, USA). Nonbevelled needles were preferred when darting from a helicopter because there was less chance of deflection with angled shots. Because of the thick skin of the rhinoceros, sufficient power was needed for the needle to cut through the skin into muscle. Therefore, a bevelled needle was preferred for ground darting. On several occasions, partial penetration occurred, resulting in s.c. injection of the immobilizing drug, due to a insufficient charge in the projectile gun or poor distance estimation. A compressed air rifle (D. L. Tranquilliser Systems) with a red dot point scope or a powder charge rifle (Pneu-Dart, Model 151C, P.O. Box 1415, Williamsport, Pennsylvania 17703, USA) with a conventional V-sight were used to propel the projectile syringes. Most rhinoceroses immobilized from the helicopter were darted in the dorsal thigh/rump area; those on the ground were most often darted in the neck/shoulder area. Ground darting of subadults or calves was carried out using either 2-ml Pneudarts (Pneudart Inc.) with 38-mm collared needles or 2–3 ml Palmer CapChur (Palmer Chemical and Capture Co.) darts with 3-

×45-mm barbed needles. Because the Pneudart could become plugged with skin, the CapChur darts were considered more reliable.

After the animal was darted, the fixed-wing aircraft or helicopter followed the animal, and if trackers or a ground crew were close, they were directed towards the rhinoceros when signs of drug effect were noticed. Once induction became evident, the pilot located a suitable landing zone and the trackers were notified by radio when the animal was in standing sedation or recumbent. After the rhinoceros became immobile (either standing or recumbent), a rope was utilized to secure the animal. With large bulls, a further 0.5–1 mg of etorphine was administered by hand-held syringe (i.m.). Sternal recumbency was preferable, but if the animal was lateral it was often impossible to move the animal to a sternal position with the limited personnel available. Once recumbent, eye ointment was applied (Bacitracin–neomycin–polymyxin ophthalmic ointment, Atlanta (Pharmaderm), Melville, New York 11747, USA), a blindfold was placed, physiological data and body and horn measurements were obtained, horn and face profiles were photographed, and blood samples and other biological data were collected. To examine the effects of immobilization on physiological parameters, a research project was implemented to evaluate the field application of pulse oximetry in rhinoceros (Allen and Boyce, unpubl. data). Animals were routinely monitored with pulse oximetry (N-10 Pulse Oximeter, Nellcor, Hayward, California 94545, USA) in 1992. The most reliable and accessible location for the pulse oximeter transducer/sensor was the ear; preparation involved scraping both sides of the ear (with a scalpel blade) close to the lower border until cartiladge was seen. A clip transducer/sensor was then applied after hemostasis was achieved. In 1992, nalorphine (10–20 mg) or nalbuphine (20–40 mg) was given i.v. as a standard procedure soon after immobilization. The dart wounds were treated with antibiotic ointment (Orbenin, Cloxacillin, Beecham Pharm., Isando, South Africa), and long-acting penicillin was administered i.m. (Tricil, Caps Veterinary, Harare, Zimbabwe). Dehorning, utilizing a 13-inch gasoline-driven chainsaw, commenced soon after recumbency once the animal was considered stable. Ear tagging and notching, painting (with white acrylic house paint) a number on the rhinoceros's back for aerial identification, and transponder placement (s.c.) in front of the left ear (Trovan, Passive Transponder System, AEG Telefunken, Frankfurt, Germany) were carried out, and on 12 animals a radio collar (Telonics Inc., Mesa, Arizona 85204, USA) was placed.

The cut horn base was painted with Stockholm tar (except on cows with calves <2 yr old), and the immobilizing agent was reversed with an opioid antagonist. In 1991, naloxone was administered i.v. at a dose range of 25–75 mg with 6–18 mg diprenorphine i.m. (naltrexone was not available in 1991). In 1992, naltrexone was administered at a dose of 25–125 mg (approximately 12 mg naltrexone/1 mg M99) i.v. Blood samples were collected soon after recumbency, and biochemical values (cortisol, creatine phosphokinase [CPK]) were determined and validated as previously reported.[17]

Data were analyzed using a statistical graphics program (Statgraphics, Statistical Graphics Corp., Rockville, Maryland 20850, USA). All data are presented as mean ± standard error of the mean (SEM). Significant differences in sample results were analyzed using an analysis of variance. All data were evaluated for distribution patterns. Induction times and CPK and cortisol values were distributed log normally and therefore were log transformed for statistical analyses.[17]

Total induction time refers to the time from dart impact to when the animal became immobile, including both recumbency and standing sedation. Tractability refers to the degree of opioid sedation and, therefore, the ability of the capture team to safely

Table 1. Values* for induction time, distance moved, and total immobilization time and physiological and biochemical data for different drug combinations used to chemically immobilize white rhinoceros (*Ceratotherium simum*) in Hwange and Matobo National Parks, Zimbabwe, 1991 and 1992.

Measurement	Etorphine/xylazine (n = 56)	Etorphine/fentanyl (n = 13)	Etorphine/detomidine (n = 60)	Etorphine alone (n = 12)
Induction (min)	6.8 ± 0.6	7.4 ± 1.3	5.6 ± 0.5	8 ± 1.6
Distance moved (km)	0.61 ± 0.05x	1.2 ± 0.17y	0.51 ± 0.06x	
Total down time (min)	41.7 ± 3.7	32.7 ± 3.6	37.2 ± 2	28.5 ± 3.4
Pulse (beats/min)	110 ± 2.9x	115 ± 5.6x	84 ± 4y	152 ± 11.6z
Respiration (breaths/min)	10.6 ± 0.47	9.6 ± 0.8	10.5 ± 0.41	11.4 ± 1
Temperature (°C)	38.1 ± 0.15	38.3 ± 0.31	37.9 ± 0.15	38.5 ± 0.25
CPK (IU/L)	158 ± 11.5x	172 ± 24x	135 ± 11y	175 ± 25x
Cortisol (μg/dl)	1.89 ± 0.14x	1.77 ± 0.12x	1.81 ± 0.32x	3.2 ± 1.5y

* Means (±SEM). Values in a row with different letters (x, y, z) are significantly different ($P < 0.05$).

handle and carry out procedures on the rhinoceros. Total down time refers to the time between dart impact and return to standing position. Reversal time refers to the time between administration of the opioid antagonist and return to standing position.

RESULTS

Of the 141 rhinoceros immobilized, 121 were adults, 10 were subadults, and 10 were calves (<3 yr old); 70 were male and 71 female.

Table 1 and Figures 1 and 2 show results of the immobilizations. The mean induction time for all drug combinations used on white rhinoceros was 6.4 ± 0.37 min (median = 5 min). There was no statistically significant difference in induction times among etorphine/xylazine, etorphine/fentanyl, etorphine/detomidine, and etorphine alone ($P > 0.05$), although etorphine/detomidine consistently produced a smoother induction. Comparison of Hwange NP data for 1991/1992 with Matobo NP data revealed a marked improvement in induction times (7 ± 0.46 min vs. 4.3 ± 0.25 min, respectively) for the Matobo operation. There was a significant difference in the distance animals moved between the drug combinations (etorphine/xylazine: etorphine 0.61 ± 0.05 km, n = 41; etorphine/detomidine, 0.51 ± 0.06 km, n = 45; etorphine/fentanyl: 1.2 ± 0.17 km, n = 12), possibly reflecting a more rapid development of incoordination with etorphine/xylazine or etorphine/detomidine. Induction in white rhinoceros was characterized by increasing incoordination with an occasional high-stepping gait. The development of signs was not as abrupt as seen with the black rhinoceros. Many animals became immobile simply because of inability to negotiate an obstacle (tree, incline). Large bulls often managed to remain on their feet and could be roped and held in standing sedation prior to processing.

In 1991, white rhinoceros were recumbent for an average of 41 ± 3.2 min (range = 16–150 min). In 1992, combining data from Hwange NP and Matobo NP, rhinoceros were recumbent for an average of 38.7 + 2.5 min, a slight improvement from 1991. Comparisons between Hwange NP (39.9 ± 2.1 min, 1991/1992) and Matobo NP (29.8 ± 1.6 min, 1992) demonstrated increased efficiency in the Matobo operation. Rhinoceros were more accessible at Matobo NP than at Hwange NP. Combined data for 1991/1992 from both parks revealed a down time of 37.7 ± 1.7 min (range = 4–150 min).

Physiological parameters were monitored in the majority of rhinoceros (Table 1). There were no significant differences in body temperature and respiration, but there was a significant difference in pulse rates ($P < 0.05$) between animals given etorphine/detomidine and those given other drug combinations (Table 1, Fig. 2). All drug combinations resulted in respiratory rates ranging from 8–12 breaths/min, but respiration was shallow and produced inadequate oxygenation. Pulse oximetry observations made on 12 immobilized (etorphine/detomidine) white rhinoceros revealed that the Sao_2 would consistently range between 40 and

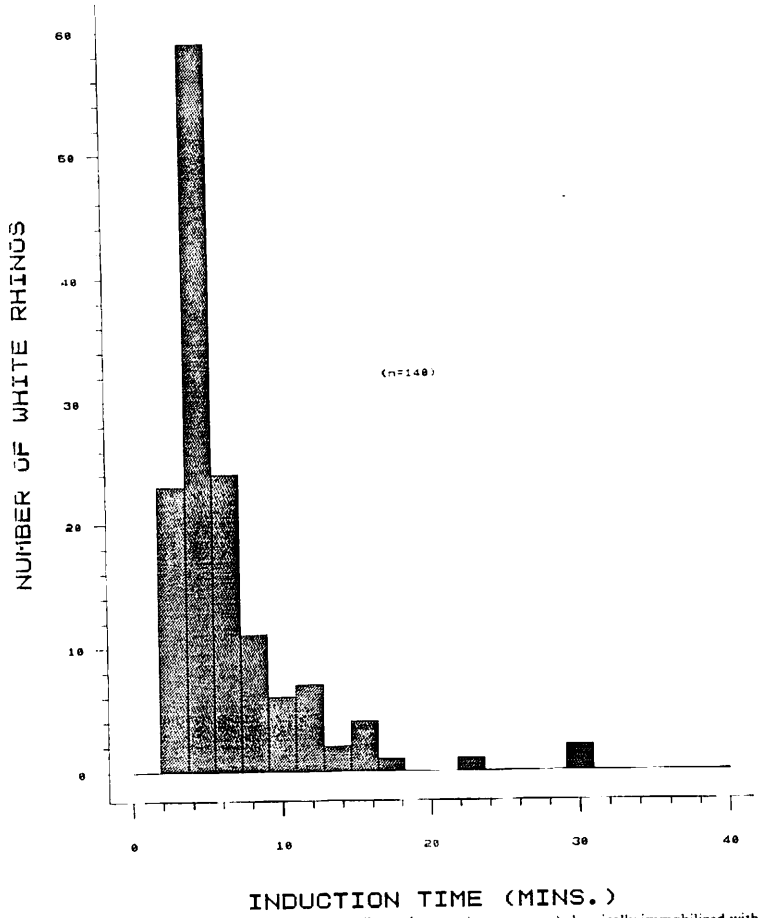

Figure 1. Induction times for white rhinoceros (*Ceratotherium simum simum*) chemically immobilized with combinations of etorphine with fentanyl, xylazine, and detomidine or with etorphine alone in Hwange and Matobo National Parks, Zimbabwe, 1991 and 1992.

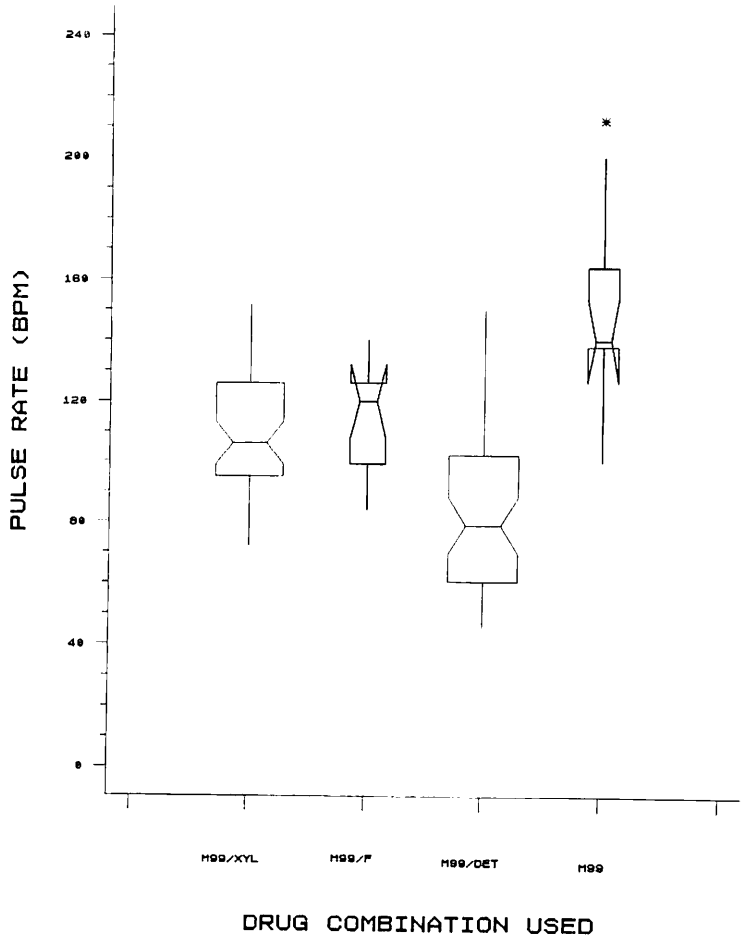

Figure 2. Notched box and whisker plots displaying pulse data (beats/min) for white rhinoceros immobilized with combinations of etorphine with fentanyl, xylazine, or detomidine or with etorphine alone. The horizontal line segment within the box is the median. The notches provide an approximate 95% test of the null hypothesis that the true medians are equal. The whiskers represent the tails of the distribution, and outside values (*) are considered outliers. There is a significant difference in pulse rates between etorphine/detomidine and the other drug combinations.

60% ($\bar{x}$ = 55%). The respiratory rate ranged from six to 10 breaths/min and heart rate was 60–100 beats/min (Allen and Boyce, unpubl. data). The use of 10–20 mg nalorphine i.v. soon after immobilization consistently improved the Sao_2 by ≥20%.

In 1991, reversal time following administration of the opioid antagonist was 92.7 ± 7 sec and reflected the specific antagonist properties of naloxone (64 ± 4 mg, n = 56) administered i.v. (combined with diprenorphine i.m., 12.4 ± 0.7 mg, n = 54). Despite this rapid arousal, reversal was often incomplete or animals showed evidence of renarcotization several hours after administration of the antagonist. Animals were noticed to be wandering or sleeping, with difficulty in arousing individuals when buzzed from the helicopter; no additional antagonists were given. The use of naltrexone (70 ± 2 mg, range = 25–125 mg, n = 68) resulted in an average reversal time of 92 ± 5 sec (n = 70), and most notable was the quality of reversal. Animals responded to immobilization reversal smoothly and consistently (within 90–100 sec) and were alert, and there was little evidence of renarcotization, although some lack of alertness has been noted elsewhere.[21]

DISCUSSION

Evaluation of the literature (1971–1993) reveals a lack of detailed analyses and appraisal of drug combinations used on free-ranging white rhinoceros, especially for extended anesthesia, although a detailed description of white rhinoceros immobilization and management has recently been reported.[21]

During the early experimental dehorning program with white rhinoceros in Hwange NP,[16] it became apparent that dehorning, with the collection of ancillary research data, required total down times of 30–40 min (Table 1). Immobilization of white rhinoceros in large numbers in 1991 allowed the evaluation of currently recommended drug combinations[4] and new combinations. Drug combinations used were etorphine and xylazine (n = 45), etorphine and fentanyl (n = 13), etorphine and detomidine (n = 1), and etorphine alone (n = 12). Hyaluronidase was mixed with all the different drug combinations to reduce induction times.[17] When hyaluronidase is used, white rhinoceros stop moving more rapidly (2–3 min) because of improved drug absorption, although they will stand and may only become recumbent in 4–6 min. In this study, the average induction time for all drug combinations (1991 and 1992) was 6.4 ± 0.37 min (median = 5 min). This result is in marked contrast to recent information and recommendations made by others[21] that induction times of <6 min constitute a potential anesthetic emergency. In fact, in field work in Zimbabwe, failure of a white rhinoceros to show signs and become recumbent in approximately 6 min is considered a potential problem. The results from 1991 suggested that the etorphine/xylazine combination was superior for induction of white rhinoceros (smooth and short time to first signs) and provided good muscle relaxation during recumbency. The initial doses of etorphine (4–5 mg) and xylazine (150–200 mg) provided rapid induction and anesthesia, characterized by a normal (under the effect of etorphine) range of respiratory rates. Thirteen animals were immobilized with etorphine (2 mg) and fentanyl (20–30 mg), a combination recommended by Natal Parks Board (NPB).[4,21] This combination produced rapid and smooth induction, although not as consistently as the etorphine/xylazine mixture. Most recumbent animals appeared relaxed, but some showed paddling movements, muscle tremor, shivering, and sweating and pulse rates were often rapid and bounding. One animal received etorphine (4 mg) and detomidine (20 mg), and although induction was rapid, anesthesia was characterized by paddling and muscle rigidity. Because this animal died just prior to reversal, this drug combination was not used again in 1991. Etorphine alone was used to immobilize young calves and some subadults (0.5–1 mg), resulting in a rela-

tively smooth and unstressful induction with good muscle relaxation. Young calves exhibited significant increases in body temperature under etorphine sedation despite cooling with water and provision of shade.

In the first 34 white rhinoceros immobilized in 1991, five mortalities occurred. Based on immobilization data subsequently collected in the latter half of 1991 and in 1992, three of these mortalities probably could have been prevented by the use of nalorphine or nalbuphine. The use of higher doses of etorphine and xylazine always carries a risk of marked respiratory depression and hypoxia. Others have reported that prolonged etorphine immobilization and recumbency were associated with hypoxemia, hypercapnia, and apparent hypertension in a white rhinoceros in captivity.[11] These problems were apparent even with low doses of etorphine (1.5–2 mg). In our study, two of the three mortalities occurred >40 min into the dehorning procedure. Mortalities occurred with etorphine/xylazine (n = 2), etorphine/fentanyl (n = 1), etorphine/detomidine (n = 1), and etorphine alone (n = 1). With all these drug combinations, the respiratory rate was within the normal range, although respiration was shallow and progressively worsening hypoxemia (congested and darkening mucous membranes) was noted in some animals (especially large bulls and cows), which was confirmed by cyanotic blood samples.

After these mortalities in 1991, the immobilizing protocol was modified slightly; the dose of etorphine was reduced by 0.5–1 mg (adult bull = 4.5–5 mg, cow = 4 mg, subadult = 2–3 mg) and the dose of xylazine by 50–100 mg (100 mg for adult bull, cow, and subadult). Immobilization of the next 37 animals was smooth and rapid, with better anesthetic stability and oxygenation (improved color of mucous membranes, evidence of improved oxygenation in blood samples collected), although despite the dosage reduction, hypoxemia was still a concern in some individuals. Etorphine in the white rhinoceros can produce significant muscle rigidity, tremors, and leg paddling, making an animal difficult to work with. It can also result in rapid body temperature rises, with an increase in oxygen demand, compounding existing hypoxemia. In 1991, the combination of etorphine and xylazine provided good muscle relaxation in the majority of animals. Reduction of the xylazine dose to below 100 mg coincided with increased rigidity and leg paddling.

Data collected and evaluated from the 1991 operation suggested that etorphine/xylazine might be superior to etorphine/fentanyl for immobilization and prolonged recumbency in the white rhinoceros. Prolonged recumbency was necessary for horn removal and data collection, but it became apparent that animals were at risk of shock and cardiovascular system collapse brought on by hypoxia. A subjective assessment of anesthesia suggested that this problem could occur under different drug combinations. Although concern was expressed with the higher drug doses (which required rapid and thorough monitoring), there were several factors that in combination could have contributed to mortality, including prolonged recumbency (>40 min) and the tendency of white rhinoceroses towards hypoventilation and hypoxemia under anesthesia, even under low doses of etorphine.[11] The massive size of the white rhinoceros (1,500–2,300 kg), with a very large digestive tract (especially the hind gut), is a significant factor in reducing the ability of the recumbent animal to oxygenate adequately over a prolonged period of recumbency. As a large perissodactylid, the white rhinoceros would be expected to experience the same adverse effects of recumbency and anesthesia observed in the horse[24] and other large mammals,[12,19] including hypoventilation, pulmonary shunting, and progressive lung atelectasis leading to associated hypoxemia and hypercapnia.[11] Clinically, the chest excursions associated with each respiratory effort appeared to be shallow, with a relatively small amount of air moved.

Pulse oximetry provided a continuous, noninvasive display of estimated arterial oxygen saturation (Sao_2) and heart rate.[26] The value of pulse oximetry in a field operation such as this came from observing trends in oxygen saturation and not from single values (Allen, pers. comm.). Monitoring of rhinoceros soon after the administration of naltrexone (i.v.) and just prior to complete arousal revealed an Sao_2 of 85–90%, which may represent approximate baseline values; Sao_2 in humans is reported as >90%.[26] Several constraints were apparent with the pulse oximeter, especially problems associated with movement of the ear, sunlight, and exudation of fluid/blood around the sensor. Careful preparation, good muscle relaxation, and shading of the ear often solved the problem. Results from these field studies confirmed previous reports that anesthesia (especially associated with prolonged recumbency) of white rhinoceros carries a risk of medical complications,[11,19] especially if the Sao_2 is 40–60% soon after recumbency and no remedial action is taken. Etorphine-induced sympathetic stimulation with peripheral vasoconstriction, tachycardia, and muscle tremors may compound hypoxemia in white rhinoceros[11] and may contribute to cardiac failure and death. Evaluation of emergency drugs in an attempt to counteract the hypoxemia indicated that 10–20 mg nalorphine (Kyron Laboratories, 20 mg/ml) administered i.v. resulted in improved respiration, with relative Sao_2 increasing. This improvement was due to the partial antagonism of etorphine, resulting in an increase in ventilatory drive and improved oxygenation. With the use of nalorphine, a >20% increase in Sao_2 was noted (Allen and Boyce, unpubl. data) and confirmed by blood samples showing a more normal color. The result was a more stable anesthesia and less risk of complications, and the pulse oximeter could be checked regularly during the dehorning; if it indicated problems, appropriate action could be taken. Administration of dopram (i.v., 400 mg) appeared to produce a small and transient improvement in the Sao_2.

Nalbuphine is equianalgesic to morphine sulfate, has significant agonist (analgesic) effects, and has antagonistic properties 25% the potency of nalorphine.[5,6,13,23] This drug was used on several white and black rhinoceros and showed promise as an alternative emergency drug to nalorphine, requiring 2–4 times the equivalent milligram dose. The use of a mixed agonist–antagonist to reverse opioid anesthesia is well established in human anesthetic practice[13] and results in reversal of depressant and sedative effects while maintaining postoperative analgesia. These effects have been tested in veterinary anesthesia.[5,6,23]

Although all the different drug combinations had resulted in rhinoceros deaths in 1991, the etorphine/detomidine mixture was considered the best. Therefore, the majority of immobilizations in 1992 were induced with etorphine/detomidine (n = 59), and a few were induced with etorphine/xylazine (n = 10). These mixtures were evaluated by combining the 1991 and 1992 data (Table 1). Although there were no statistically significant differences in induction times among the three drug combinations (excluding etorphine alone), etorphine/detomidine induction was smoother and appeared to be more rapid (Table 1) and the quality of anesthesia was excellent based on pulse rate, pulse oximetry (Sao_2) with nalorphine or nalbuphine i.v., muscle relaxation, and absence of rigidity/paddling. Rhinoceros immobilized with etorphine/detomidine had pulse rates significantly lower than did those immobilized with the other two combinations and etorphine alone (Table 1). The pulse was normal, as was auscultation of the heart, indicating good cardiac output. The pulse rate with etorphine/fentanyl was rapid and bounding. The body temperature associated with etorphine/detomidine immobilization was lower than that associated with the other combinations, probably as a result of good muscle relaxation and absence of paddling. CPK values indicated that the etorphine/detomidine combination produced less muscle damage, probably as

a result of rapid induction, absence of paddling, and good muscle relaxation. This result has been seen with modifications of drug dosages used on the black rhinoceros.[17] Cortisol values were significantly higher in calves and subadults immobilized with etorphine alone. Young animals have a tendancy to become excited, especially after their mothers have been immobilized. Ground darting of these young animals, next to their mothers, is carried out with minimal disturbance, but stress is experienced prior to immobilization, as has been reported with black rhinoceros subadults and calves.[17] With adults, positioning appeared to be important in reducing paddling and muscle tremors; sternal recumbency until complete relaxation occurs is preferable.

With large adult bulls, a dose of 4.2 mg etorphine combined with 16 mg detomidine produced good anesthesia, but the head was often held up with some rigidity of the neck muscles. For example, by adding 5 mg detomidine i.v. (total dose = 20–22 mg) there was a noticeable relaxation in the head stance in one large bull. Manipulation of the etorphine dose in some animals from 4 mg to 4.2 mg, while maintaining the sedative dose, produced noticeably significant changes in quality of anesthesia. An increase of 0.2 mg etorphine resulted in poorer muscle relaxation and increased head shaking and jerking, with dehorning which made the dehorning operation more difficult. A reduction of 0.2–0.4 mg etorphine resulted in a significantly more relaxed animal. Additional doses of etorphine administered to an immobilized captive white rhinoceros exacerbated muscle trembling and central nervous system excitement.[11] Elsewhere in southern Africa, midazolam (Dormicum, Roche Laboratories, Isando, Republic of South Africa) has been administered i.v. (20–40 mg) to white rhinoceros when muscle relaxation has been poor and has produced excellent relaxation and may be a useful adjunct to etorphine/detomidine anesthesia postimmobilization in the white rhinoceros (Morkel, pers. obs.).

Reversal of etorphine with its standard opioid anatagonist agent diprenorphine often results in incomplete antagonisn in the white rhinoceros[21] and use of nalorphine (up to 250 mg) has been recommended.[4] With diprenorphine, rhinoceros often are depressed, wander aimlessly for several hours, and do not respond well to adverse stimuli. The reason for this partial antagonism is not clear (diprenorphine works well with the black rhinoceros) but may be related to the fact that deprenorphine is not a pure opioid antagonist and has agonist properties. Opioid recycling may be a contributory factor.[1] Complete antagonism is important, especially when dealing with cow/calf combinations. Young calves (<12 mo old) are vulnerable to predation by hyenas (*Crocuta crocuta*) and lions (*Panthera leo*) if separated from their mothers. If either mother or calf is unable to respond to a threat due to partial narcosis, there would be a high risk of the calf being killed and/or the mother injured. Naloxone produced a smooth and rapid reversal in the white rhinoceros, but its short half-life, combined with problems associated with deprenorphine reversal (i.e., return of sedative effects), resulted in incomplete antagonism with time in a significant number of rhinoceros. In 1992, naltrexone was evaluated as an antagonist for etorphine. Like naloxone, naltrexone is a pure antagonist, producing complete reversal of the opioid effects. The advantage of naltrexone is that the half-life is 12–24 hr. It should therefore prevent opioid recycling, with less chance of complications with cow/calf combinations. Between 50 and 75 mg of naltrexone i.v. was adequate for reversing 4–4.5 mg of etorphine (approximately 12.5 mg naltrexone to 1 mg etorphine). On occasion, 125 mg was given, but the results were no better than those for lower doses. In some white rhinoceros given naltrexone, sedative signs may return.[21] It is unclear whether this is due to effects of detomidine (when used in combination) or to renarcotization. In Matobo NP, the average reversal time using naltrexone was 104 ± 7 sec (range – 55–215 sec, n – 31), with a reversal time for rhinoceros in both parks of 92 ± 5 sec, n = 70. The time to arousal was very consistent (90–100 sec), which was important with cow/calf combinations. The calf was always given the reversal agents 20 sec before the mother, which ensured that the calf stayed near the mother and they both left the scene together. If the mother was aroused before the calf she would leave the scene without the calf, especially if the reversal was incomplete and the cow was disorientated.

CONCLUSIONS

Critical evaluation of various drug combinations used to chemically immobilize white rhinoceros during a conservation dehorning program in Zimbabwe has enabled more specific recommendations to be made as to choice of drug combinations. Although etorphine/xylazine, etorphine/fentanyl, and etorphine/detomidine produce similar induction times, the immobilization with etorphine/detomidine appears to be smoother and more rapid. If the immobilization is to be quick (<30 min) and easily reversed, all combinations could be recommended as effective and safe. Hyoscine mixed with the opioid, as recommended by the NPB, does not appear to be necessary, and its use questionable.[4,16,18,21] A higher dose of etorphine ensures smooth and rapid induction in the white rhinoceros, reducing stress and chances of trauma, but partial antagonism of the opioid must be carried out to ensure adequate oxygenation during prolonged immobilization and recumbency. The quality of anesthesia with etorphine/detomidine especially with regards to muscle relaxation, tractability, and pulse rate, was superior to that of the other combinations, especially for prolonged immobilization. All drug combinations produced degrees of cardiovascular and respiratory system compromise, evidenced by low SaO_2. High doses of etorphine and detomidine should be used with caution when ground-darting free-ranging animals without air support or experienced trackers. Inability to locate an immobilized white rhinoceros within 40 min may predispose the animal to hypoxia and cardiovascular collapse.

In light of these field results, a dose rate of 3.0–4.0 mg etorphine (subadult to large bull) combined with 12–20 mg detomidine and hyaluronidase (1,500 IU) is recommended for the chemical immobilization of the white rhinoceros. Large bulls may require supplementation with etorphine (0.5 mg) on the ground. A standard protocol should involve the administration of 10–20 mg nalorphine (or 20–40 mg nalbuphine) i.v. as soon as possible after recumbency, which will counteract respiratory depression and hypoxemia, resulting in an increase of at least 20% in Sao_2 within 5 min. This protocol will not result in arousal, and the quality of anesthesia will remain excellent. Midazolam (20–40 mg, i.v.) may be indicated as an adjunct to etorphine/detomidine when improved muscle relaxation is required. Reversal of the opioid with 50–75 mg naltrexone i.v. is recommended. It may be necessary to consider using 100–150 mg naltrexone to prevent some of the sedative signs seen after reversal. In any case, reversal time will be consistent, and reversal will be complete.

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