

CASE REPORT

Overdose during chemical restraint in a black rhinoceros (*Diceros bicornis*)

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Abstract

A juvenile female black rhinoceros (*Diceros bicornis*) was successfully treated after overdose of drugs used for chemical restraint. Subsequent general anaesthesia for surgical reduction of a recurrent rectal prolapse was uneventful. Over a 25-minute period before transportation to the veterinary hospital, the animal received a total dose of 1.225 mg etorphine, 30 mg acepromazine and 30 mg detomidine. Based on an *estimated* mass of 200 kg, these corresponded to doses of $6.1 \mu\text{g kg}^{-1}$ etorphine, $150 \mu\text{g kg}^{-1}$ acepromazine, and $150 \mu\text{g kg}^{-1}$ detomidine which constitutes considerable overdose for each drug given separately, notwithstanding the synergy that probably resulted when the three drugs were present concurrently. The estimated body mass may have substantially overestimated the actual body mass and exacerbated overdosage. The animal was recumbent and apnoeic on arrival at the hospital. Heart sounds were auscultated and a weak peripheral pulse was palpated; no pulse deficits were detected, although the heart rate was low. The trachea was intubated, inspired breath was enriched with oxygen and the lungs ventilated manually. Diprenorphine (1.5 mg) was given intravenously and spontaneous breathing resumed 11 minutes later. After induction of general anaesthesia using isoflurane, emergency surgery for correction of rectal prolapse was performed, from

which the animal recovered uneventfully. The case highlights some of the practical problems that may be encountered in dealing with dangerous and unfamiliar species.

Keywords anaesthesia, resuscitation, overdose, rhinoceros.

Introduction

The chemical immobilization and anaesthesia of free-ranging rhinoceros species has been described (Harthoorn 1962; Nelson & Fowler 1986; Kock et al. 1990, 1995; Raath 1999; Stegmann et al. 2001). However, little information is available on anaesthesia of captive rhinoceros, or on their anaesthetic management under hospital conditions (Radcliffe et al. 2000a,b; Atkinson et al. 2002). This case report describes treatment of inadvertent overdose of drugs that had been used for chemical restraint in a captive-bred, juvenile female black rhinoceros (*Diceros bicornis*).

Case report

Between 170 and 226 days of age, the rhinoceros had undergone three unsuccessful attempts to surgically repair a severely traumatized third degree rectal prolapse; several different approaches had been used to immobilize the animal for these procedures (Table 1). At 230 days of age the animal

Table 1 Summary of immobilisation drugs administered to a black rhinoceros at 170, 177, 226 and 230 days of age

Age (days)	Estimated weight (kg)	Etorphine		Acepromazine		Detomidine		Morphine		Effect observed
		Dose (mg)	Dose ($\mu\text{g kg}^{-1}$), based on estimated weight	Dose (mg)	Dose ($\mu\text{g kg}^{-1}$), based on estimated weight	Dose (mg)	Dose ($\mu\text{g kg}^{-1}$), based on estimated weight	Dose (mg)	Dose ($\mu\text{g kg}^{-1}$), based on estimated weight	
170	150	-	-	-	-	7.5	50	-	-	Ambulatory and tractable
177	150	-	-	-	-	8	53	-	-	Ambulatory after detomidine alone.
	-	-	-	10	68	-	-	50	330	Recumbent, able to intubate the trachea
226*	200	-	-	-	-	12	60	-	-	Still lively, but could separate from mother
	-	-	-	10	50	9	45	60	300	Standing, but quiet enough to permit extradural lumbosacral injection
230	200	1.225	6.1	30	150	30	150	-	-	Collapse

*Supplemented by lumbosacral epidural anaesthesia (bupivacaine 50 mg, morphine sulphate 10 mg).

was chemically restrained and transported from the referring institution to the veterinary teaching hospital for a fourth attempt at surgical correction of the prolapse.

Before dosing for chemical restraint, the animal had been estimated to weigh 200 kg and it was intractable and belligerent. To facilitate transportation, etorphine hydrochloride (1.225 mg) and acepromazine maleate (5 mg) (Large Animal Immobilon; C-Vet Veterinary Products, Lancashire, UK) were administered intramuscularly (IM) by dart. Fifteen minutes later, the animal was given IM detomidine (25 mg) (Domosedan; Pfizer Animal Health, Kent, UK) and acepromazine (15 mg) (ACP 10 mg mL⁻¹; C-Vet Veterinary Products). A further 10 minutes later, more detomidine (5 mg) and acepromazine (10 mg) were administered IM. The animal was then transported in a crate in the back of a van, where it was not observed.

On arrival at the hospital, approximately 50 minutes after the initial injection of etorphine and the first acepromazine dose, the animal was laterally recumbent, unconscious and in respiratory arrest; its mucous membranes were cyanotic. The heart rate (by thoracic auscultation) was 53 beats minute⁻¹. Palpation of the auricular artery revealed a regular but weak arterial pulse.

The trachea was intubated with a 60-cm long 14 mm id endotracheal tube (Phoenix; Arnolds Veterinary Products, Shrewesbury, UK) under direct vision with the aid of a laryngoscope fitted with a 30-cm Miller pattern blade (Arnolds Veterinary Products). In order to facilitate orotracheal intubation, the jaws were held open with the aid of two lengths of tape, one each across the maxillary and mandibular interdental spaces and pulled dorsally and ventrally respectively. Manual intermittent positive pressure ventilation (IPPV) was started immediately with 100% oxygen delivered via a Boyle Mark IV circle system (BOC Medical, Guildford, Surrey, UK) at 8–10 breaths minute⁻¹. Diprenorphine (1.5 mg) (Revivon; C-Vet Veterinary Products, Lancashire, UK) was administered into a marginal auricular vein. A pulse oximeter (S-100; Simed, Miami, FL, USA) was applied to the tongue where S_pO₂ was found to be 93% soon after IPPV was started. Venous access was established using a 20G Teflon over the needle catheter passed into an auricular vein. Hartmann's solution (Isolec; Ivex Pharmaceuticals, Larne, UK) was administered intravenously at 30 mL kg⁻¹ hour⁻¹ based on the estimated mass. Once an airway had been established, IPPV initiated and circulatory

support provided, the animal was unloaded from the transportation crate.

Arterial blood pressure was measured indirectly using an oscillometric device (Dinamap; Critikon, Tampa, FL, USA) with the cuff (Adult, Dura-Cuf; Critikon, Tampa, FL, USA) placed around the mid antebrachium. Mean arterial pressure was 46 mmHg. The base-apex electrocardiograph was displayed on a medical oscilloscope (Minimon; Kontron Instruments, Hertfordshire, UK) and no obvious abnormalities were observed.

Spontaneous respiratory efforts resumed 11 minutes after diprenorphine injection and the initiation of IPPV. By this time, haemoglobin saturation had risen to 98%, heart rate had increased to 78 beats minute^{-1} and mean systemic arterial pressure was 51 mmHg.

It was felt that delay would render the prolapse inoperable, hence general anaesthesia was induced using isoflurane in oxygen via the circle breathing system, and preparation for surgical correction was commenced immediately.

The animal breathed spontaneously throughout 170 minutes of general anaesthesia. Systemic arterial blood pressure was supported with Hartmann's solution (Isolec; Ivex Pharmaceuticals, Larne, UK; $10\text{--}30\text{ mL}^{-1}\text{ kg}^{-1}\text{ hour}^{-1}$ IV) and dobutamine (Dobutrex; Eli Lilly & Co Ltd, Hampshire, UK) infused to effect ($60\text{--}250\text{ }\mu\text{g minute}^{-1}$). For 2 hours mean systemic arterial blood pressure was maintained at approximately 65 mmHg, after which it decreased to below 55 mmHg and was unresponsive to dobutamine. Phenylephrine was administered (initially at $100\text{ }\mu\text{g minute}^{-1}$ and then titrated to effect) and the mean arterial pressure increased from 39 to 69 mmHg over 5 minutes and was maintained between 55 and 75 mmHg until the end of the procedure. Carprofen (Rimadyl; Pfizer Animal Health; 200 mg, IV) was administered just before the end of surgery.

After surgery all monitoring devices and the venous catheter were removed. This was a precaution in case recovery was unexpectedly rapid. Isoflurane was discontinued, the animal loaded into its crate and transported while still unconscious. Oxygen was administered during transportation using a demand valve until the rhinoceros attempted to swallow, at which time the orotracheal tube was removed – approximately 12 minutes after cessation of isoflurane administration. The animal recovered quickly and smoothly, and was on its feet within 20 minutes of discontinuing isoflurane. By

this time it was aggressive, alert, responsive and moving confidently. The animal was closely observed for 12 hours after return to the zoo. Its behaviour was judged to be normal throughout this time.

Discussion

The combination of etorphine ($1.7\text{--}2.9\text{ }\mu\text{g kg}^{-1}$) with acepromazine ($16.9\text{--}50.0\text{ }\mu\text{g kg}^{-1}$) has been used in adult black rhinoceros ($400\text{--}1196\text{ kg}$ body mass), with and without azaperone ($0.19\text{--}0.50\text{ mg kg}^{-1}$), to produce chemical restraint or recumbency, with 'induction' times of up to 42 minutes, and rapid recovery following antagonism with nalorphine (Harthoorn 1975). Etorphine (at approximate doses of $1.6\text{ }\mu\text{g kg}^{-1}$) in combination with detomidine (approximately $5.2\text{ }\mu\text{g kg}^{-1}$) has been used for the immobilization of adult wild white rhinoceros (*Ceratotherium simum*) weighing up to 2500 kg (Kock *et al.* 1995). While there are no published reports on the use of etorphine and detomidine in black rhinoceroses, the safe use of etorphine (3.0 mg) in combination with another α_2 -agonist, xylazine (100 mg), has been reported in adult black rhinoceroses (Kock *et al.* 1990). Before leaving the zoo, the juvenile subject of the current report received 1.225 mg etorphine, 30 mg acepromazine and 30 mg detomidine. Based on an *estimated* mass of 200 kg, these correspond to doses of 6.1, 150 and $150\text{ }\mu\text{g kg}^{-1}$ of etorphine, acepromazine and detomidine, respectively (Table 1). Each normalized dose is at least several fold greater than those previously reported in rhinoceroses; this suggests that this animal's collapse was the result of overdosage of each drug and that this was exacerbated by a summation or synergism of drug effects.

Although the true body mass of this animal was not known, another female black rhinoceros, a half sibling of the one reported here and also reared at the referring institution, had a body mass of 149 kg at the same age as the subject of this paper. If the mass of the rhinoceros was actually closer to 149 kg, rather than the estimate of 200 kg, then this error alone would have created 34% overdosage and further aggravated the effects of excessive normalized doses.

Etorphine with acepromazine can take up to 25 minutes to produce recumbency in black rhinoceros (Harthoorn 1975). In this animal, all of the etorphine, acepromazine and detomidine were given within 25 minutes of the initial dose, suggesting that the additional drugs were given without

permitting previous doses to reach maximal effect. This probably contributed to an accumulative effect of acepromazine and detomidine.

When the subject arrived at the hospital it was obviously in need of emergency treatment. An airway, IPPV and circulatory support were provided promptly and before unloading from the transportation crate.

Reduced ventilatory drive is the primary sign of overdose with OP3 agonists, hence it is likely that etorphine was primarily responsible for the apnoea observed at presentation. Etorphine causes bradycardia and hypotension in dogs, and tachycardia and hypertension in horses (Schlarmann *et al.* 1973) and white rhinoceros (le Blanc *et al.* 1987; Heard *et al.* 1992); its cardiovascular effects in black rhinoceroses have not been reported. The bradycardia observed when this subject arrived at the hospital could be attributed to detomidine, which, in common with other α_2 -agonists, is associated with bradycardia in other species (Alitalo 1986; Salonen *et al.* 1989). Acepromazine is an α_1 -adrenoceptor antagonist and, as such, may have been largely responsible for the hypotension that was observed at admission.

Specific antagonists are available for etorphine, detomidine and acepromazine. Diprenorphine, an antagonist at OP3 receptors, has been used to reverse the effects of etorphine in rhinoceroses (Alford *et al.* 1974; Kock *et al.* 1990, 1995; Raath 1999). This drug was administered because it was easily available and a satisfactory dose in black rhinoceros is documented. The specific α_2 -adrenoceptor antagonist, atipamezole, was considered for reversing the detomidine, an α_2 -agonist. However, atipamezole was not given because a documented dose for black rhinoceros was unavailable, and because the response to diprenorphine and other resuscitation measures was satisfactory. Phenylephrine is an α_1 -adrenoceptor agonist and, as such, can be used to reverse the vasodilatation (but not the CNS depression) caused by acepromazine; we did not use phenylephrine during initial treatment because the hypotension responded to other resuscitation efforts; nevertheless, phenylephrine was used during subsequent general anaesthesia to treat hypotension that did not respond to intravascular fluids and dobutamine.

The information from this case supports the assertion that isoflurane is a useful agent for prolonging anaesthesia in rhinoceroses (Cornick-Seahorn *et al.* 1995; Seliskar *et al.* 2000). Recovery was rapid, smooth and complete. Therefore, it can

be concluded that the drugs used to immobilize the animal for transportation and examination almost 4 hours earlier, had been mostly redistributed, metabolized or antagonized.

In conclusion, this animal presented with profound cardiopulmonary depression induced by overdose of etorphine, detomidine and acepromazine. This overdosage was caused by inappropriately large normalized doses of each drug, overestimation of body mass, 'top up' doses that were given before preceding doses had reached maximal effect, and the additive and interactive effects of the drugs. This report illustrates some of the practical problems inherent in managing dangerous, nondomestic species and highlights the pitfalls in anaesthetising animals for which reliable preoperative physical data are unavailable. When undertaking the chemical immobilization of such an animal, the literature should be searched for documentation of all doses, sufficient time should be permitted for each drug to reach maximal effect, drugs with specific antagonists should be used, and appropriate doses of those should be to hand. In addition, animals that have been given immobilizing drugs should be observed continuously until they have fully recovered.

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