Standing sedation with medetomidine and butorphanol in captive African elephants (*Loxodonta africana*)

I. Lüders [a,b], B. Tindall [c], D. Young [d], G. van der Horst [a,b], S. Botha [e], I. Luther [a,b], L. Maree [a,b], H. J. Bertschinger [f,*]

[a] *Department of Medical Biosciences, University of the Western Cape, Private Bag X17, Bellville 7535, South Africa*
[b] *National Zoological Gardens of South Africa, 323 Boom Street, Pretoria 0110, South Africa*
[c] *Robberg Veterinary Clinic, 56 Longships, Plettenberg Bay 6600, South Africa*
[d] *African Elephant Research Unit, Plettenberg Bay, South Africa*
[e] *African Lion Safari, 1386 Cooper Road, Cambridge, ON, N1R 5S, Canada*
[f] *Section of Reproduction, Faculty of Veterinary Science, University of Pretoria, Private Bag X04, Onderstepoort 0110, South Africa*

* Corresponding author. Tel.: +27 12 8043312
E-mail address: henkbert@tiscali.co.za (H.J. Bertschinger).

Abstract

Doses for standing sedation allowing for various procedures in otherwise inaccessible, untrained captive African elephant bulls are presented. Thirty-three standing sedations were performed in 12 males aged 8 to 30 years (1-4 sedations per animal). Each bull received a combination of 0.009 ± 0.002 mg/kg medetomidine and 0.03 ± 0.007 mg/kg butorphanol. Full sedation was reached on average 25.5 min after injection. The addition of hyaluronidase (1000-2000 IU) significantly reduced time to full sedation to 16.5 min (paired *t* test, *P*= 0.024). Reversal was induced with intramuscular atipamezole 0.008 (± 0.002) and naltrexone 0.035 (± 0.015) mg/kg. Recovery took on average 7 min (3-18 min). The medetomidine/butorphanol combination provided safe standing sedation for smaller procedures.

Keywords: Elephant bull; Butorphanol; Medetomidine; Hyaluronidase

When training or adequate handling facilities (such as a restraint chute) are lacking, chemical restraint becomes an option for accessing and handling elephants more safely for selected procedures. Many drugs are in use for chemical restraint in elephants (Table 1) but standing sedation is considered to pose a lower risk to captive elephants compared to general anaesthesia. It also allows access to both sides of the animal and, in general, elephant care staff find it more acceptable (Neiffer et al., 2005). The α_2-adrenoceptor agonists, such as xylazine and detomidine, in combination with either ketamine or butorphanol have been used for standing sedation in African elephants (Table 1) but the use of medetomidine, a more potent and safe α_2-agonist, has so far only been reported for Asian elephants (Sarma et al., 2002).

The aim of this study was to define doses of medetomidine and butorphanol combinations to achieve safe and effective standing sedation in captive African elephant bulls of different ages in order to perform procedures like semen collection and transrectal ultrasound examinations.

Twelve captive bulls, 8-30 years old, from four facilities in South Africa were used in the study (Table 2). Shoulder height was measured during each sedation and mean weight was calculated from this value using four different, previously published formulas (Johnson and Buss, 1965; Hanks, 1972; Laws et al., 1975). The bulls were sedated once (n=4), or three to four times (n=8) over a period of 3 years. All procedures were carried out in accordance with the Animal Use and Care Committee of the University of Pretoria (permit V016-12; 24 April 2012).

Table 1

Overview of previously published sedative, anaesthetic and reversal drugs used in adult African and Asian elephants. Doses are given in mg/kg unless otherwise stated. Drug effects may differ based on age, sex, body condition and health status of the elephant. Modified from Fowler and Mikota (2006).

Drugs used for chemical restraint	Purpose, action	Dose (mg/kg) for:			Comments
		Sedation	Full immobilisation	Route	
Ketamine	Non-narcotic sedative	Not used alone in elephants		IM	Only in combination with tranquilizer or α_2-agonist
Xylazine	Sedative, α_2-agonist	0.08-0.1	0.15-0.2	IM	Best in combination with ketamine or butorphanol
Detomidine	Sedative, α_2-agonist	0.0055		IM	**Asian elephant only**
Medetomidine	Sedative, α_2-agonist	0.04-0.08		IM	
Butorphanol	Immobilizer, opiate	0.01-0.03		IM	
Etorphine	Immobilizer, opiate		0.0015-0.003	IM	Usually in combination with azaperone or α_2-agonist
Azaperone	Short-acting tranquilizer	0.056-0.107		IM,IV	
Azaperone/ butorphanol	Standing sedation	Azaperone: 0.12 Butorphanol:10 mg total dose		IM	Single report
Xylazine/ butorphanol	Standing sedation	0.035-0.16 0.005-0.036		IM or IV	Use lower dose for IV administration
Xylazine/ ketamine	Standing sedation or full immobilization	0.1 ± 0.04 0.6 ± 0.13	0.2 1.0-1.5	IM	
Detomidine/ butorphanol [a]	Standing sedation	0.013–0.02 0.013–0.02		IM	1:1 ratio (50-70 mg total dose for each drug)
Diprenorphine	Opioid receptor antagonist	0.0083 ±0.001			
Naltrexone	Opioid receptor antagonist	1 mg/1mg narcotic		IM	
Naloxone	Opioid receptor antagonist	0.004		IM	or 10-50 mg total dose
Atipamezole	α_2-adrenerdgic antagonist	1 mg/10 mg xylazine		IM or slow IV	
Yohimbine	Xylazine antagonist	0.05-0.13		IV	

IM, intramuscular; IV, intravenous

[a] Neiffer et al. (2005)

Table 2

Total anaesthetic and reversal drug doses per elephant for 33 standing sedations performed in 12 male African elephants once or 3-4 times over a 3-year period.

Elephant bull				Sedation		Top-up		Reversal			
Number	**Age (years)**	**Calculated weight (kg)**	***n*=**	**Medetomidine (mg)**	**Butorphanol (mg)**	**Medetomidine /butorphanol (mg)**	**Time (min) [a] /route**	**Time to reversal (min)[b]**	**Atipamezole (mg)**	**Naltrexone (mg)**	**Route**
1	19	2662	1	20	85			55	20	100	IM
2	8	1657	1	20	50			90 [c]	25	50/100	IV, IM
3	10-13	1994-2316	3	14-20	40-60	8/25	25/IM	74	15-25	80-150	IM
4	23-26	4230-5029	4	21-50	100-150	8-10/25	30/IV	74	25-40	100-250	IV, IM
5	23-26	4147-4935	4	20-50	100-200	10/25	2/IV	83	30-40	100-250	IV, IM
6	23-26	4443-4843	4	50-55	100-135	10-15/25	25-30/IV	108	20-40	100-150	IV, IM
7	25-28	4172-4336	4	35-50	100-145	10/20	25 /IV	61	30-35	100-150	IM
8	24-27	3595-4025	4	25-40	75-100			63	25-35	100-150	IM
9	17-21	2401-3197	3	15-30	70-100	5/10	25/IV	69	20-25	80-100	IV, IM
10	12-15	2124-3232	3	10-30	40-100			64	10-25	60-100	IM
11	20	3033	1	40	75	10/25	26/IV	86	20	100	IV, IM
12	30	5815	1	50	150			58	25	150	IV, IM
		Mean dose mg/kg		**0.009**	**0.030**				**0.008**	**0.035**	
			SD	**± 0.002**	**± 0.007**				**± 0.002**	**± 0.015**	

IM, intramuscular; IV, intravenous

[a] Time from injection of first bolus to injection of top-up

[b] Time from injection of first bolus to injection of reversal drugs

[c] This bull (number 2) was given a reversing agent after 90 min following collapse onto his carpal joints

A combination of medetomidine (20 mg/mL, Kyron Laboratories) and butorphanol (50 mg/mL, Kyron Laboratories) were drawn up into one syringe. Males were either guided into a restraint chute or pen system, where they were injected IM by hand, or were darted while free-standing outside and only restrained thereafter.

When the tip of the elephant's trunk was fully relaxed and resting on the ground, attempts to access the animal began. If, after 30 min, the elephant was still responsive to handling of the tail, or the trunk was not permanently resting on the ground, or leg movements were present, an IV or IM top-up was given (Table 2). During the last round of sedations (*n*=8) 1000 to 2000 IU hyaluronidase (Hylase, 5000 IU per vial, Kyron Laboratories) were added to the cocktail to promote rapid drug resorption. For reversal of the sedations, naltrexone (Trexonil, 50 mg/mL, Wildlife Pharmaceuticals) and atipamezole (Antisedan, 5 mg/mL, Zoetis) were administered IM or partially IV in separate syringes.

Table 2 shows the drugs and dosages used to sedate and reverse each of the 12 bulls treated 1-4 times. The mean intervals from injection until the first observed effect were 7.7 min (5-12 min) without hyaluronidase and 12 min (5-30 min) after the addition of hyaluronidase. Average time to full sedation was 25.5 min (10-52 min) without hyaluronidase. The addition of hyaluronidase significantly reduced the time to full sedation to 16.5 min (12-33 min). The statistical analysis was performed using GraphPad InStat Version 3 software for a paired *t* test (*P*=0.024; df=7; *n*=8 bulls).

For 11 sedations in seven bulls, a top-up dose was needed 25-30 min after administration of the initial bolus (Table 2). Mean total duration of sedation required for all

procedures to be completed was 75 ± 20 min (48-110 min). In a single case, the youngest elephant (number 2) partially collapsed onto his carpal joints about 85 min after administration of the sedative drugs (Table 2). The drug was immediately reversed with 25 mg atipamezole and 50 mg naltrexone IV and an additional 100 mg naltrexone IM. He regained his footing rapidly and was fully conscious after 3 min.

All sedations were partially or completely reversed with IM atipamezole and naltrexone (Table 2). On seven occasions, one-third of the dose was given IV and the remainder given IM. In both cases, full recovery was achieved quickly and took on average 7 ± SD 4 min (2.5-18.0 min).

The results show that the combination of medetomidine (0.009 ±SD 0.002 mg/kg) and butorphanol (0.03 ±SD 0.007 mg/kg) provided a safe and reliable method for standing sedation of African elephant bulls after an induction period of 20 - 30 min. A supplemental injection of 0.003 ±SD 0.001 mg/kg medetomidine and 0.007 ±SD 0.003 mg/kg butorphanol was required for each of the 11 procedures. Induction times were significantly reduced when 1000-2000 IU hyaluronidase were added to the drug combination. This enzyme is used to facilitate drug resorption during wildlife immobilizations (Morton and Kock, 1991). Medetomidine is the most potent of the α_2-adrenoreceptor agonist family with more specific actions on receptors associated with sedation and analgesia (Fowler and Mikota, 2006). Previously, however, only detomidine in combination with butorphanol in a 1:1 ratio has been described for African elephants (Neiffer et al., 2005; Table 1).

The mean dose of medetomidine administered in combination with butorphanol in this study was almost twice the dose used for captive Asian elephants (Sarma et al., 2002) in

which acceptable standing sedation was achieved using medetomidine alone. Asian elephants appear to be far more sensitive to the α_2-agonists. For example, the recommended dose for detomidine in Asian elephants is 0.0055 mg/kg (Fowler and Mikota, 2006), whereas African elephants require 0.013-0.02 mg/kg (Neiffer et al., 2005; Table 1).

All of our elephants were able to walk out of the restraint pen or chute within 10-15 min after administration of the antidotes. The reversibility of both drugs used in the present study is a great advantage over drug combinations that include ketamine or azaperone, which have no reversal agent. Adverse gastrointestinal side effects (such as bloat or mild colic), as have been described after similar sedations in African elephants (Neiffer et al., 2005), were not seen. The only side effect we observed was increased salivation in all bulls.

In conclusion, this study determined an effective and fully reversible combination dose of medetomidine and butorphanol required to achieve standing sedation in African elephant bulls. The inclusion of hyaluronidase in the sedative cocktail significantly reduced the induction time.

Conflict of interest statement

None of the authors of this paper has a financial or personal relationship with other people or organisation that could inappropriately influence or bias the content of the paper.

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