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## EFFECTS OF PHYSIOLOGICAL STATE ON DURATION OF SEDATION IN SOUTHERN ELEPHANT SEALS

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**ABSTRACT:** One hundred eighty-one female and thirteen postweanling pup southern elephant seals (*Mirounga leonina*) were sedated using a combination of ketamine hydrochloride and xylazine hydrochloride. Physiological state had a profound effect on response of the animals to sedation. Physiologically stressed postlactation and postpartum cows had significantly longer periods of sedation than pre-molting females or recently weaned pups. Induction time was not affected by physiological status. Dose rates are recommended for elephant seals in various physiological states.

**Key words:** Southern elephant seal, *Mirounga leonina*, ketamine hydrochloride, xylazine hydrochloride, sedation, physiological states, field study.

### INTRODUCTION

Differences in intraspecific sensitivity to ketamine hydrochloride (KT), reflected by wide variation in dose rates, have been described in many species (Booth, 1982). However, there is little information on intraspecific sensitivity of KT in pinnipeds although several authors have noted a wide variation in response (Geraci, 1973; Briggs et al., 1975; Engelhardt, 1977). This is despite its generally wide use (Briggs et al., 1975; Kooyman et al., 1980; Geraci et al., 1981; Ryding, 1982; Trillmich, 1983; Baker and Gatesman, 1985; Gales and Burton, 1987). In addition to individual sensitivity, Gales and Burton (1987) have suggested that physiological status may be an important factor affecting drug response in the southern elephant seal (*Mirounga leonina*). This paper presents data on changes in duration of sedation of southern elephant seals in different physiological states when sedated with KT and xylazine hydrochloride (XL). Guidelines for the use of KT and XL are established as based on these findings.

### MATERIALS AND METHODS

During the austral summer of 1987-1988, 194 southern elephant seals were sedated, some repeatedly, using KT (186 mg/ml) (Parke Davis, Sydney, New South Wales, Australia) in combination with XL (100 mg/ml) ("Rompun 100,"

Bayer Australia, Botany, New South Wales, Australia) as part of an energetics study of this species on Macquarie Island (54°30'S, 158°54'E). Atropine sulfate (0.65 mg/ml) (Parnell Laboratories, Kirrawee, New South Wales, Australia) was included in the combination to decrease upper respiratory tract secretions and prevent bradycardia which may predispose the animal to enter its dive response when sedated. All cows received a total dose of 1.3 mg atropine whereas weanlings received 0.65 mg. A level of sedation was achieved such that the animals could be rolled onto a sling, weighed and blood samples collected.

Animals at four stages of their life cycle were sedated: (1) postpartum cows within 1 day of giving birth; (2) postlactational cows, circa 20 days postpartum; (3) pre-molting cows, recently hauled ashore to molt; and (4) pups, within 2 days of weaning. Animals in stages (1) and (2) were under considerable physiological stress due to parturition and negative energy balance, while those in stages (3) and (4) were under only slight physiological stress and had large fat reserves to sustain them through a subsequent fast.

Initially, dose rates were estimated from the length-mass relationship suggested by Ling and Bryden (1981). Despite this relationship tending to underestimate mass and resulting in the administration of relatively low doses of sedatives, prolonged periods of deep sedation were produced. The duration and degree of sedation were greater than required to weigh, measure and obtain blood samples from the animals. The quantity of sedative was then decreased for subsequent seals until a level and duration of sedation was found that allowed safe handling of the animal with minimal drug usage. Dose rates were calculated in this manner for seals in each

TABLE 1. Mean, standard deviation and range of body mass, dose rate of ketamine, dose rate of xylazine, induction time, and duration of sedation for elephant seals in four physiological states.

Measurement	Value	Physiological state			
		Postpartum	Late-lactation	Pre-molt	Weanlings
Mass (kg)	mean	470.6	334.0	406.0	113.9
	SD	68.4	47.0	74.9	17.5
	max.	568.0	334.0	546.0	155.0
	min.	285.0	261.0	261.0	89.0
Ketamine (mg/kg)	mean	3.92	2.99	3.71	3.29
	SD	1.50	0.58	1.14	1.15
	max.	6.96	4.28	7.49	5.22
	min.	1.86	2.41	1.91	1.60
Xylazine (mg/kg)	mean	0.55	0.92	0.72	0.73
	SD	0.20	0.14	0.20	0.26
	max.	1.05	1.15	1.15	1.12
	min.	0.25	0.78	0.37	0.36
Induction time (min)	mean	10	11	8	8
	SD	5	4	3	3
	max.	20	20	14	15
	min.	3	6	1	5
Duration time (min)	mean	139	112	66	33
	SD	92	42	30	28
	max.	369	185	123	115
	min.	47	62	15	9
	<i>n</i>	19	8	30	13

of the groups and used as a basis to sedate other animals in each group. Sedatives were administered to cows using the remote injection technique (Ryding, 1982). Pups and weanlings were manually restrained, and the drugs given into the extradural vein or the epaxial musculature. Responses were predictable in animals given intravenous injections and variable if given intramuscularly because of difficulty in placement within a poorly developed muscle mass.

Sedative induction time was defined as the time from injection until the animal failed to respond to head patting. Duration of sedation was defined as the time from induction until the animal could raise its head.

## RESULTS

The mean masses, dose rates of KT and XL, induction times and duration of sedation for seals in each of the four states are listed in Table 1.

The mean mass of seals in all four groups were significantly different (one-way ANOVA,  $F_{3,66} = 90.062$ ,  $P < 0.001$ ). Postpartum cows were heaviest, followed by the pre-molt cows. The postlactation cows were

approximately 30% lighter than those immediately postpartum.

The mean dose of KT ( $3.61 \pm 1.25$  mg/kg) did not vary significantly among the groups (one-way ANOVA,  $F_{3,66} = 1.490$ ,  $P > 0.05$ ). There were differences in the dose rates of XL among the groups (one-way ANOVA,  $F_{3,66} = 6.424$ ,  $P < 0.05$ ). There were no significant differences in XL dose rates among postlactation cows, pre-molt cows and weanlings, but the dose rate of XL for postpartum cows was significantly lower (SNK test; Zar, 1984). The mean amount of XL given to pre-molting cows, postlactation cows and weanlings was  $0.75 \pm 0.22$  mg/kg; postpartum animals received  $0.55 \pm 1.5$  mg/kg.

Induction time did not vary among the groups of seals (one-way ANOVA,  $F_{3,66} = 2.20$ ,  $P > 0.05$ ). The overall mean induction time was  $9.1 \pm 3.7$  min. Duration of sedation varied significantly among groups of seals (one-way ANOVA,  $F_{3,66} = 11.782$ ,  $P < 0.01$ ). Student-Newman-Keuls anal-

ysis (Zar, 1984) revealed that duration of sedation of weanlings and pre-molt cows were not significantly different from each other, but were significantly lower than postpartum cows, and postlactation cows.

The duration of anesthesia for postpartum cows did not differ significantly from that for postlactation cows, in spite of the postpartum cows having received less XL than the other groups. The mean duration of sedation for weanlings and pre-molt cows was  $56.2 \pm 33.4$  min, while that for postpartum and postlactation cows was  $131.1 \pm 83.1$  min.

Blanket dose rates of KT, XL and atropine found to be effective were: for postpartum and pre-molt cows 3 ml (300 mg) XL, 8 ml (1,488 mg) KT and 2 ml (1.3 mg) atropine, postlactation cows 3 ml (300 mg) XL, 6 ml KT and 2 ml (1.3 mg) atropine, and weanlings 1 ml (100 mg) XL, 1 ml (186 mg) KT and 1 ml (0.65 mg) atropine).

Of 226 episodes of sedation, fatalities occurred on eight occasions representing a mortality rate of 3.5%. One postpartum cow had her skull crushed by a bull during recovery from sedation. Two postpartum animals appeared to recover uneventfully from sedation, but one animal was found dead 48 hr later, the other 96 hr later. Another animal sedated for 6 hr died 18 hr postinduction. Before death there were prolonged periods of gasping mouth breathing. Tachycardia, cyanosis and decreased peripheral perfusion also were evident. The cause of death could not be established in these animals. Two pups and two cows died showing clinical signs of hyperthermia.

#### DISCUSSION

Previous studies on the sedation of elephant seals have used length-mass regressions to calculate dose rates of anesthetic drugs (Ryding, 1982; Gales and Burton, 1987). Length-mass regressions have been shown to be inaccurate when estimating the actual mass of the seal, which can lead to wide discrepancies in dose rates. Also,

dose rates based on length-mass regression curves do not take into account the physiological status of the animal although this consideration has been recommended (Gales and Burton, 1987).

Our study shows the physiological status of an animal has a profound effect on its sensitivity to sedatives. There were no significant differences in the dose of KT or induction time, but there were large differences in duration of immobilization among the four physiological states examined. Newly weaned pups and pre-molt cows (representing animals under minimal physiological stress) had durations of one half that of the more stressed postpartum and postlactation cows, despite the fact that postpartum animals received significantly less XL.

Due to the onset of bradycardia and hypotension following the use of XL in other animals (Gleed, 1987), lower doses were used in postpartum cows. We further suspected that higher doses may affect thermoregulation (Vergani, 1985) and may predispose animals to enter a dive response.

With the exception of postpartum cows, the proportion of XL was increased and so allowed the quantity of KT to be reduced. Thus, a lower dose of KT was used than previously described by other workers using this combination (Gales and Burton, 1987).

The elephant seal changes its total body mass markedly through loss or gain of fat in different physiological states; but its lean body mass changes only fractionally (Bryden, 1969). Lean body mass as a percentage of total body mass is lowest in fat postweaning pups, increasing through postpartum and pre-molt cows to a maximum in lean postlactation cows. As the poorly vascularized blubber has little effect on KT concentration in the blood (Ryding, 1982), an increase in drug concentration at the biophase will occur as the percentage fat increases (Briggs et al., 1975). Thus, it is likely that weanlings received the highest dose at the biophase,

followed by postpartum cows, pre-molt cows and postlactation cows. If the extent of distribution (and thus concentration at the biophase) alone were the major determinant of duration of anesthesia, duration should be longer in fatter animals (weanlings, postpartum and pre-molt cows compared to postlactation cows). However, this is not the case as weanlings and pre-molt cows had much shorter duration times.

Differences in distribution of anesthetic during different physiological states will influence biophase drug concentration and may account for differences in duration of action. As drug effect is more closely correlated with plasma concentration of the drug than with the administration dose (Levy, 1968), and induction times did not vary significantly, it is likely that the rate of redistribution from central to peripheral compartments varies among seals in different physiological states. The rate of redistribution being faster as the relative proportion of fat increases.

Elimination rates of the drugs may also account for differences in duration of sedation. Physiological state may change the ability of an animal to metabolize sedatives. Biotransformation by the hepatic microsomal mixed function oxidase system constitutes the principal process of elimination of the highly lipid-soluble KT (Baggot, 1978). It is possible that in postpartum and postlactation animals, the mixed function oxidase system is being flooded by products of an already highly stressed metabolism which are competing for KT. This would decrease elimination rate by way of a change from first order kinetic to dose dependent elimination.

In other species there are marked differences in the processes of elimination, and rapid development of enzyme systems during the neonatal period (Baggot, 1978). In some species it has been shown that the blood brain barrier is not as well developed in neonates as in adults and this may result in a more rapid induction of sedation (Meyer, 1987). The shorter duration of anesthesia seen in weanlings (Table 1) may

be due to smaller body mass, greater fat content and percentage liver mass (Bryden, 1971) resulting in more rapid and efficient redistribution and elimination of sedatives.

It is also possible that the different responses may be due to inherent differences in drug-receptor tissue sensitivity with different physiological states. The relationship between sedation and physiological status in the elephant seal appears to be complex. It is apparent that physiological status has a significant effect on response of the animal to sedatives and must be taken into consideration when calculating dose rates when coupled with the inability to accurately predict masses of animals. Sedation of the southern elephant seal offers a unique problem to the anesthetist. This study has overcome these problems by offering blanket dose rates of sedatives based primarily on physiological status with mass taken into account rather than based upon mass alone.

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