

Prolonged chemical restraint of walrus (*Odobenus rosmarus*) with etorphine supplemented with medetomidine

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ABSTRACT

Physiological studies involving the use of isotopic water required chemical restraint of free-ranging walrus (*Odobenus rosmarus*) for several hours. In August 2000, six male walrus (total body mass: 1050–1550 kg) were immobilized in East Greenland by remote delivery of 8.0–9.8 mg of etorphine and subsequently restrained for up to 6.75 h by administration of medetomidine. The effects of etorphine were reversed with 10–24 mg diprenorphine. After termination of the etorphine-induced apnoea, lasting an average of 15.8 min (SD = 9.7, range = 9.5–35.2 min, n = 6), the animals were initially given 10–20 mg medetomidine intramuscularly. The initial dose was further augmented by 5 mg at intervals of 5 min. In two cases, when medetomidine was administered through a catheter inserted in the extradural vein, the animal became instantly apnoeic and regained respiratory function only after intravenous injection of the prescribed dose of the antagonist atipamezole and of the respiratory stimulant doxapram. After an average of 3.5 hours of immobilisation, rectal temperature began to increase and it is conceivable that this is the factor that will ultimately limit the duration of immobilisation. The animals became conscious and fully mobile shortly after an intravenous injection of a dose of atipamezole approximately twice the mass of the total dose of medetomidine given during the procedure followed by 400 mg of doxapram. It is concluded that medetomidine appears to be a suitable drug for chemical restraint of walrus for time-consuming procedures following initial immobilisation by etorphine. With animals of total body mass around 1,000–1,500 kg, the drug should be given intramuscularly in 10–20 mg increments (total mass 10–60 mg) until the breathing rate falls to approximately 1 min⁻¹. At this level, breathing is maintained and animals do not respond to touch or injection.

INTRODUCTION

A variety of drugs or drug combinations has to date been used to immobilize walrus (*Odobenus rosmarus*) in the field, including phencyclidine and acepromazine (DeMaster *et al.* 1981), tiletamine and zolazepam (Stirling and Sjare 1988; Hills 1992; Griffiths *et al.* 1993), etorphine (Hills 1992; Born and Knutsen 1992; Griffiths *et al.* 1993; Acquarone *et al.* 2014) and carfentanil (Hills 1992; Lanthier *et al.* 1999). None has proven ideal for prolonged immobilization. Only Lydersen *et al.* (1992) have tried a prolonged immobilisation of walrus. The animal was initially immobilized by

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intramuscular (i.m.) administration of 5 mg ($5.2 \mu\text{g} \cdot \text{kg}^{-1}$) etorphine. The effect of the etorphine was reversed, as prescribed, by its antagonist diprenorphine. To keep control over the animal, a combined dose of 80 mg medetomidine and 1000 mg ketamine was then administered, before complete recovery, and provided restraint for further 5 h. (Lydersen *et al.* 1992). An investigation of body water dynamics and energy expenditure in walrus in Greenland using isotope-labelled water (Acquarone *et al.* 2006; Acquarone and Born 2007) created the need to regularly immobilize and restrain the subjects for longer than typical to allow the injected isotopes to mix with the body water pool.

MATERIALS AND METHODS

The fieldwork was conducted at a haulout at Lille Snenæs (Dove Bay, Greenland; $76^{\circ}52.7'N$, $19^{\circ}37.9'W$) during August 2000. The site is a small sandy tombolo with an axis of about 50 m joining a low rocky outcrop to the coast. Sea access is on both sides and walrus typically haul out on the south-eastern side in groups of up to 16 adult and subadult males. Females or young were not detected during this study. Weather conditions were fine during the immobilizations: dry weather, $+3$ to $+7^{\circ}\text{C}$; wind force 1 to 4 m sec^{-1} ; sunny or overcast.

Six adult male walrus were used in this study. Total body mass (TBM) was measured for one animal (Walrus 2) or estimated from measurements of standard body length and axillary girth using the equations in Born *et al.* (2003) and ranged from 1,050 to 1,550 kg. All were immobilized by remote administration of a dart containing 8.0–9.8 mg etorphine (“M99”, $9.8 \text{ mg} \cdot \text{ml}^{-1}$, Vericore Ltd., Dundee, Scotland) as described in Griffiths *et al.* (1993) and Acquarone *et al.* (2014). Etorphine was antagonized by hand delivered i.m. injections of 6–15 mg of diprenorphine (“M5050”, $12 \text{ mg} \cdot \text{ml}^{-1}$, Vericore Ltd., Dundee, Scotland) in the posterior dorsal region. Three of the animals were immobilized for the first time (animals 1-3: Table 1); one had been immobilized previously twice in 1989 and once in 1990 (animal 4: Table 1), and the last two (animals 5, 6: Table 1) had been immobilized previously three times and twice respectively during the same month.

The etorphine/diprenorphine protocol used for immobilisation of all walrus is described in detail in Acquarone *et al.* (2014, this volume). In this report we only present information on a sub-set of six walrus that were treated with medetomidine after they had received etorphine and diprenorphine. In brief, the animals did not receive any premedication and were chosen for their calm behaviour and placement favourable to darting. Onset of tremors a few minutes after darting with etorphine indicated the end of the induction phase, the time for delivery of diprenorphine and the possibility to approach. All

Table 1. Data on the use of etorphine/diprenorphine for the immobilisation of six walruses that were further kept restrained by use of medetomidine/atipamezole directly after regaining full respiratory function.

Animal no.	Day (Aug 2000)	ID Code	TBM* (kg)	Etorphine	Apnoea		Diprenorphine		
				Amount (mg)	Start**	Duration (min)	1st inj.**	Amount 1st inj. (mg)	Amount total (mg)
1	5	2000-3	1,050	9.8	2.0	9.5	4.7	14.4	17.4
2	9	2000-6	1,090	9.8	1.9	10.3	5.3	12.0	12.0
3	15	2000-8	1,300	9.8	3.5	11.8	8.5	10.0	10.0
4	18	1989-3	1,550	9.8	3.8	35.2	8.3	12.0	12.0
5	19	2000-4	1,280	8.0	3.7	14.7	7.6	12.0	24.0
6	22	2000-2	1,250	8.0	4.6	13.5	7.3	12.0	12.0

(*) = Total Body Mass

(**) = Minutes from darting with etorphine

animals showed a variable apnoeic period starting at the end of the induction phase during which they were intubated to facilitate the resumption of breathing. Breathing in the period following the first administration of diprenorphine was forced: deeper and considerably faster than pre-immobilisation.

Some 30–40 min after the resumption of breathing, when the respiratory rate had fallen to around 8 min⁻¹ and was not longer forced, six walruses started to emerge from immobilisation, as seen by beginning to open their eyes and move their head, which rendered venous access impossible. At this point they were given an intramuscular injection of 10–20 mg medetomidine (“Domitor Forte”, 10mg · ml⁻¹, Orion Pharma, Turku, Finland) (in the first animal only, a mixture of medetomidine and ketamine) every 5 min until they again were sufficiently sedated to allow the placement of a catheter (Becton-Dickinson Secalon-T, 2.0mm x 160mm, Medisinsk Utstyr AS, Oslo, Norway) into the extradural intravertebral sinus for blood sampling. In two cases, medetomidine was also given intravenously (i.v.). A 25 cm-long luer-lock extension set (Becton-Dickinson Connecta, Medisinsk Utstyr AS, Oslo, Norway) was attached to the indwelling catheter to facilitate blood sampling with minimum disturbance to the animal. The catheter and extension were flushed with heparinized saline following each blood sampling. For two walruses plasma was collected and sent to Orion Pharma, Turku, Finland, for medetomidine level determination. Body temperature was measured using an electronic thermometer (DM852, Ellab, Copenhagen, Denmark) with a probe inserted approximately 20 cm in the rectum. Heart rate was monitored with an electronic pulse meter (Exersentry, Respiration Instruments, Inc.,

Monroeville, Pennsylvania 15146, U.S.A.) equipped with four sensors connected to 6 cm long needles inserted, as far as possible from each other, through the skin. The animals' head was covered with a towel to shade the eyes from direct sun light and prevent visual stimuli during handling.

If an animal showed signs of arousal (head lift, body movement), it was given additional medetomidine i.m. or i.v. At the conclusion of the sampling period the walrus was given the α_2 antagonist atipamezole ("Antisedan", 5 mg · ml⁻¹, Orion Pharma, Turku, Finland) at a rate of approximately twice the mass of the total medetomidine administered. The dose was given either half intravenously (i.v.) and half i.m., or wholly i.m. If an animal went into apnoea after the administration of medetomidine, it was given i.v. atipamezole at a rate of twice the mass of medetomidine injected, followed by 400mg of the respiratory stimulant doxapram ("Dopram", Wyeth Lederle, USA) also i.v.

RESULTS

Six walruses received i.m. medetomidine following reversal of the etorphine with diprenorphine (Table 1). In the search for the most appropriate prolonged immobilisation method two of these six animals were at some stage given medetomidine i.v., but in both cases this led to immediate apnoea that could only be reversed by the antagonist atipamezole (discussed below). The first of the six animals received a combination of ketamine and medetomidine (see below, Animal 1). This animal also stopped breathing, and breathing resumed only after i.v. injection of atipamezole and doxapram. All subsequent animals received only medetomidine i.m.

Walrus 1 (estimated TBM: 1,050 kg) received 9.8 mg etorphine that was reversed with 14.4 mg diprenorphine (Table 1). Drug-induced apnoea lasted a total of 9.5 min and the animal was breathing in a controlled and regular manner at 17 min post darting. (All records of time are time in relation to initial impact of the dart containing etorphine unless otherwise stated.) This animal was given 24 mg medetomidine and 260 mg ketamine i.m. at 1.28 h post-darting and at 1.33 h ceased breathing. At 1.42 h it was given 70 mg atipamezole with 400 mg doxapram i.v. and resumed breathing 2 min later. It remained totally immobile for the next 25 min, when it stopped breathing again. This time, however, it could be aroused enough for head-lifting and breathing by physical stimulation of the muzzle, after which it would again lower its head and become apnoeic. It was aroused in this way every two minutes to breathe until 2.68 h, when it was given a further 50 mg atipamezole i.m. At 2.72 h it resumed spontaneous breathing, but otherwise lay immobile. At 2.97 h a blood sampling was attempted, but this aroused the animal totally and stimulated it to enter the sea. It was recaptured five days later and from

observations made before the new immobilisation it behaved normally. Six days later it was observed once again by the haulout.

Walrus 2 (measured TBM 1,090 kg) was immobilized with 9.8 mg etorphine that was reversed with 12.0 mg diprenorphine. Drug-induced apnoea lasted 10.3 min and the breath became regular at 14 min post darting (Table 1). This walrus received 10 mg medetomidine i.m. at 35 min with no observable effect on breathing, and a further 5 mg i.m. at 45 min, which resulted in the breathing becoming shallower, interspersed with occasional deep breaths. Immobilisation was sufficient to allow the walrus to be rolled onto a scale and weighed. By 2.37 h it had begun to move its flippers and body and was given 5 mg medetomidine i.v. It stopped breathing almost immediately, however, and at 2.43 h was given 40 mg atipamezole and 500 mg doxapram i.v. At 2.50 h it arose, with apparent full reversal of all immobilization, entered the sea and strongly swam away. This animal was recaptured both 3 and 13 days later and in both occasions it behaved normally.

Walrus 3 (estimated TBM 1,300 kg) received 9.8 mg etorphine and 10.0 mg diprenorphine. Duration of drug-induced apnoea was 11.8 min and the animal was breathing regularly at 21 min post darting (Table 1). Walrus 3 was given 10 mg medetomidine at 39 min (with no effect) and a further 5 mg at 44 min, after which the breathing rate fell from 12 to around 4 min⁻¹. The walrus remained immobile for the next 2.5 h, after which it began to rock its torso and move its head with breathing. At 3.53 h and again at 3.62 h it received 5 mg of medetomidine i.m. after which it again lay still with regular breathing. At 6.67 h it was given 30 mg atipamezole i.m., and four minutes later it sat up and went into the sea, apparently fully awake. Walrus 3 was recaptured three days later, and also three times the following year. On every occasion it behaved normally.

Walrus 4 (estimated TBM 1,550 kg) received 9.8 mg etorphine and 12.0 mg diprenorphine. Drug-induced apnoea lasted 35.2 min and regular breathing was resumed 44 min post darting (Table 1). This individual received 12 mg medetomidine i.m. at 1.00 h and a further 3 mg i.m. at 1.08 hr. Thereafter it lay immobile with regular breathing until about 1.50 h, when it began to move its torso and rear flippers intermittently. It did not react, however, to insertion of a needle into the extradural space for blood sampling and was not given additional medetomidine. At 2.88 h it sat up abruptly and entered the sea, apparently totally recovered and without the use of atipamezole. This animal had been already immobilized by etorphine darting both in 1989 and 1990 and was also immobilized twice the following year (2001).

Walrus 5 (estimated TBM 1,280 kg) received 8.0 mg etorphine and 24.0 mg diprenorphine. Drug-induced apnoea lasted 14.7 min and at 18.5 min post

darting the walrus had resumed regular breathing (Table 1). Walrus 5 received 20 mg medetomidine i.m. at 30 min. At 45 min it showed some body-rocking, and reacted to the insertion of a rectal thermometer and to tapping on a tusk, and was given a further 10 mg medetomidine i.m. at 1.06 h. At 1.83 h it was given 5 mg medetomidine i.v. and stopped breathing almost immediately. Several minutes later breathing had not recommenced and there was no response to the i.v. injection of 500 mg doxapram. At 1.90 h it was given 25 mg atipamezole i.v. Shortly after it again began to breathe at a rate of about 1 min^{-1} , but continued to lie immobile without response to tactile stimulation. After 15–20 min this respiratory pattern became Cheyne-Stokes-like, with 3–5 deep breaths every couple of minutes. Approaching 5 h immobility, the breathing pattern reverted to a regular one, about 1 min^{-1} . At 5.48 h the walrus was given 50 mg atipamezole, half i.m. and half i.v., and at 5.53 h it sat up and entered the sea of its own accord, apparently normal. Even though this animal was not seen at haulout later this season, its movements have been followed by satellite tacking for more than 100 days after this immobilization without any sign of abnormal behaviour.

Walrus 6 (estimated TBM 1,250 kg) received 8.0 mg etorphine and 12.0 mg diprenorphine. Drug induced apnoea lasted 13.5 min and the animal was breathing regularly at 21 min post darting. This animal was given 20 mg medetomidine i.m. at 40 min, 45 min and 55 min, a total of 60 mg. After the third dose its breathing rate fell from 6 min^{-1} to $1\text{--}2 \text{ min}^{-1}$. As with walrus 5, its breathing changed to a Cheyne-Stokes-like pattern, with several good breaths every 1.5–2.5 min (Fig. 1). The heart rate altered cyclically with the breathing, from typically around $30\text{--}45 \text{ min}^{-1}$ between breaths to $65\text{--}70 \text{ min}^{-1}$ just prior to and during breathing. At 3.42 h the animal showed signs of arousal, with some body-rocking and flipper movement, and shorter intervals between breaths. At 4.23 h and 4.32 h it lifted its head and moved a little forwards, but otherwise continued to lie quietly. At 4.78 h it was given 100 mg atipamezole i.m., and at 4.88 h it sat up and entered the sea without apparent sedation. Walrus 6 was a frequent occupant of the haulout the following year when it was immobilized further 3 times and on every occasion it behaved normally.

The duration of immobilisations ranged from 2.36 h to 6.75 h. In all cases except one in which the animal suddenly arose and entered the sea without receiving the antagonist, arousal was induced by injection of atipamezole.

Plasma medetomidine concentration was measured by the producers of the drug (Orion Pharma, Turku, Finland) in animals 5 and 6. In both animals, concentration was initially low, and then increased to variable levels during the following hours (Table 2). There was no apparent consistent trend in plasma medetomidine concentration with time, but it is worth noting that the

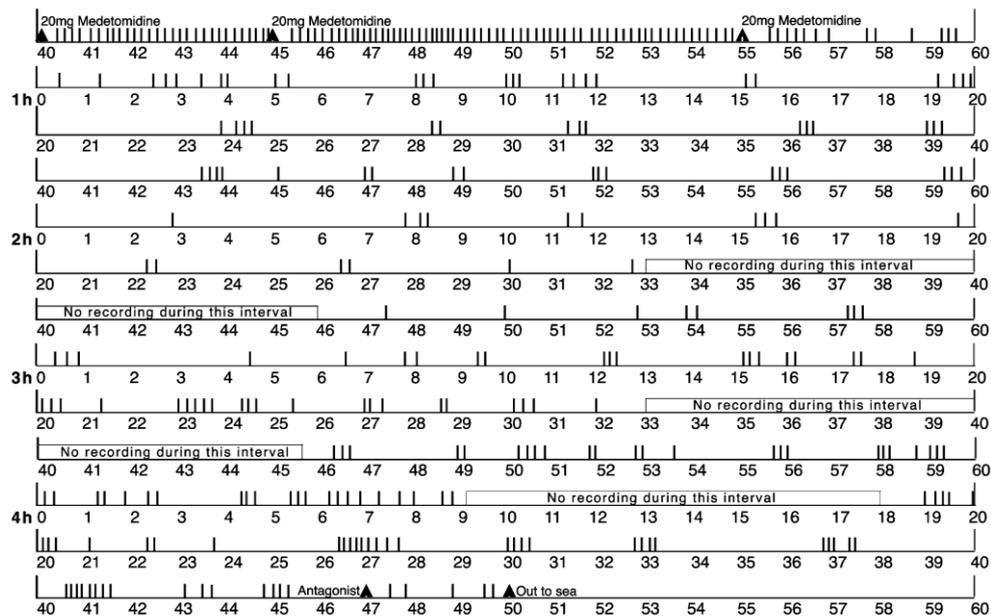


Fig. 1. Breathing rate of an adult male walrus (no. 6) during immobilisation with medetomidine following an initial immobilisation with etorphine/diprenorphine. Time (min) is given relative to darting with etorphine (i.e. the first dose of medetomidine was injected 40 min after darting). The breathing rate was greatly reduced after the third medetomidine injection, and after a further 0.5h was transformed into a more intermittent pattern with several breaths at intervals of several minutes.

concentration did not decline with time and was still high at the time of reversal of the drug.

Table 2. Medetomidine concentrations in blood plasma of two adult male walrus in relation to time during immobilisation involving the initial use of etorphine/diprenorphine.

Time after Etorphine darting (h)	Plasma Medetomidine concentration (ng ml ⁻¹)	
	Walrus 5	Walrus 6
0.5 (before)	Undetectable	
1.5	No sampling	2.81
2.0	No sampling	19.7
2.5	9.24	18.6
3.0	9.82	13.7
3.5	5.11	9.42
4.0	12.1	9.66
4.5	11.5	15.0
5.0	6.33	
5.5	5.54	

Rectal temperature was measured in animals 3, 4, 5 and 6 (Fig. 2). Rectal temperature shortly after initial immobilisation with etorphine ranged 35.8 to 37.0 °C, and remained below 38.0 °C for some 2–3 hr. Thereafter there was a tendency for the rectal temperature to increase slowly to around 38 °C, although it never approached 42 °C at which protein denaturation and thus permanent cellular damage occurs in mammals (Imrie and Hall 1990).

DISCUSSION

The choice of employing medetomidine for restraint after immobilisation by etorphine was taken after considerations on employing medetomidine as the immobilizing agent instead of etorphine. However, initial trials in 1999 with medetomidine and Telazol® in two animals proved fatal in both cases (Griffiths unpublished) and indicated that this combination is not suitable for immobilisation without extensive testing. Considering the small walrus populations on both Greenland and Spitsbergen, it was decided not to risk more casualties and to revert to the familiar immobilisation drug, etorphine, as the first drug.

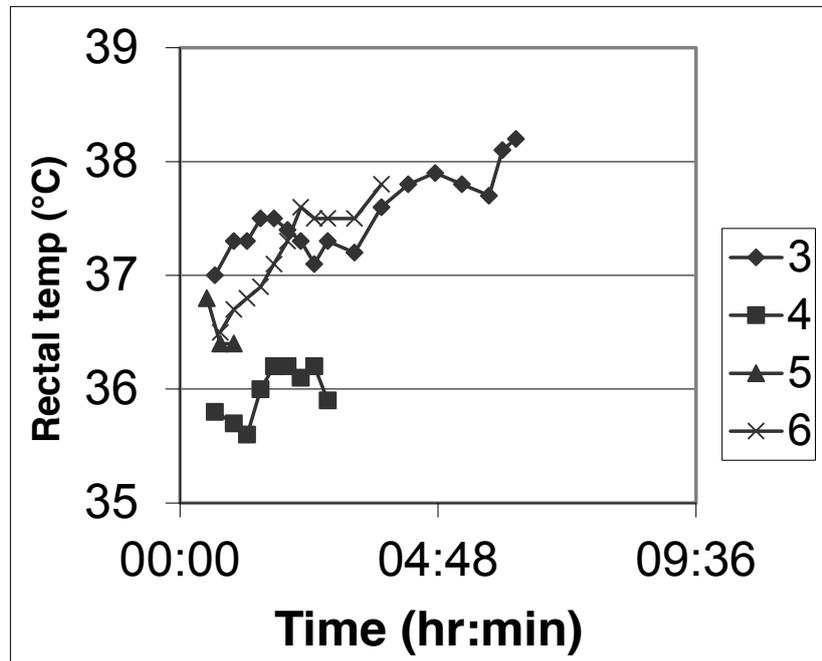


Fig. 2. Rectal temperature in relation to time (min after darting with etorphine) in four adult male walrus that were immobilized with medetomidine.

Medetomidine appeared to be suitable as an agent for immobilisation maintenance, following etorphine, when prolonged immobilisation of walrus is necessary. When the animal appears to have recovered from the initial etorphine drugging and is breathing regularly and unlaboured at a rate of 6–8 min^{-1} (which for the animals in this study was at about 35–40 min from darting) it may be given medetomidine, using respiratory rate and pattern as an indicator of depth of anaesthesia. Medetomidine is to be given i.m. at 5–20 mg increments every five minutes until the respiratory rate falls to approximately 1 min^{-1} . The amount of medetomidine required to achieve this effect ranged in this trial between 15 and 60 mg. In the two animals immobilized the longest (5 and 6), the breathing pattern subsequently changed to an intermittent type, with bursts of several breaths interspersed with periods of apnoea up to 4 min in duration.

The variation in recovery time after etorphine immobilisation (Table 1) may indicate residual central nervous system depression, which in turn may influence the amount of medetomidine needed to re-immobilize the animals. The large variation in the dose of medetomidine needed to immobilize the walrus (15–60 mg or 9.7–22.9 $\mu\text{g} \cdot \text{kg}^{-1}$) is therefore probably related to the effects of the initial etorphine drugging. However, there is potential imprecision in the estimated TBM and the precise fat content of the animals

is unknown, making calculation of dosage of any agent by metabolic weight difficult.

There was considerable variation in the duration of medetomidine immobilisation before additional medetomidine was needed (2.0–3.5 hrs). Repeated dosage should be administered i.m. and in small increments, with respiratory rate again being the key indicator of level of sedation. Signs of arousal from sedation included rocking of the torso in association with breathing, movement of the rear flippers, head movement and increased respiratory rate to at least one breath per minute. These signs are similar to those observed after reversal of etorphine with diprenorphine in which some walrus quickly become mobile and enter the sea of their own accord, reacting aggressively to human proximity. Others will recommence breathing and show head-lift, but appear unwilling to ambulate, do not respond to physical contact other than with head-lift, and may remain in the same position for over a day.

In all cases intravenous administration of medetomidine, even a dose as small as 5 mg, led to immediate cessation of breathing as previously reported (Lydersen *et al.* 1992). Only the use of the antagonist atipamezole could start breathing again. We conclude after several attempts to administer medetomidine i.v. that this route is absolutely contraindicated in the walrus, at least following the use of etorphine.

In all cases, rectal temperature remained nearly unaltered for a couple of hours of immobilisation (Fig. 2). No attempts were made to cool the animals or otherwise regulate body temperature during immobilization. There was a trend for temperature to increase with prolonged immobilisation to around 38 °C by the time the immobilisation was reversed. Whether rectal temperature would have continued to increase or have levelled off is unknown. The fact that the rectal temperature increased in the three animals monitored for more than two hours indicates that medetomidine may impair thermoregulation in walrus.

All these animals apparently did survive and were observed directly or followed through satellite tracking several weeks and even a year after immobilisation. This procedure did not seem to have a significant impact on their survival. Despite the survival of the immobilized animals in this case study, prolonged anaesthesia had profound effects on the ventilation of these animals and therefore does represent a risk. None of the data presented here enable us to evaluate the effect of prolonged immobilisation on the O₂ and CO₂ levels in these animals. Blood gas analysis or indirect method (ex: capnometry) could provide useful information but was not possible in this situation. Supplemental oxygen was not used to improve the oxygenation,

also due to logistical restrictions, but its importance in the treatment of animals with marked depressed ventilation is acknowledged and we recommend its use.

In summary, medetomidine appears to be a suitable drug for immobilisation of walrus for time-consuming procedures following initial capture with etorphine and reversal with diprenorphine. With animals weighing 1,000–1,500 kg, the drug should be given intramuscularly in 5–20 mg increments (total mass 10–60 mg) until the breathing rate falls to approximately 1 min⁻¹. At this level, breathing is maintained and animals do not respond to touch or injection. A rectal thermometer should be used, since after several hours of immobilisation rectal temperature begins to increase and it is conceivable that this is the factor that will ultimately limit the duration of immobilisation possible. Finally the evaluation of the severity of hypoxia and hypercapnia is recommended as is the use of supplemental oxygen to reduce the severity of both.

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