

Medetomidine-tiletamine-zolazepam in brown bears (*Ursus arctos*): Test of high doses in captive animals

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Introduction

In the Scandinavian Brown Bear Project, medetomidine (M¹) in combination with tiletamine-zolazepam (TZ²) has been used for immobilization and anaesthesia of free-ranging brown bears since 1992. In total, 818 captures have been carried out with the MTZ combination (Arnemo et al., 2001; Arnemo et al., 2003; Arnemo & Brunberg, unpublished data). Currently the following standard doses are used for immobilization of free-ranging bears in April-May: Yearlings (15-45 kg) 1.25 mg M + 62.5 mg TZ; small bears (2-3 years, 45-70 kg) 2.5 mg M + 250 mg TZ; adult females and small males (70-120 kg) 5 mg M + 250 mg TZ; adult males (120-200 kg) 10 mg M + 500 mg TZ; large males (> 200 kg) 15 mg M + 750 mg TZ. The M:TZ ratio is kept constant so that doses can be split or combined. For reversal, atipamezole (A³) at 5 mg per mg M is used i.m.

TZ used to be the drug of choice for immobilization of several bear species (Kreeger et al., 2002; White et al., 1996; Gibeau and Paquet, 1991; Stirling et al., 1989). TZ has a wide margin of safety, and has no major cardiopulmonary or thermoregulatory side effects in bears. The main disadvantage of TZ is extended recoveries. There is no reversal agent for tiletamine, and the use of a benzodiazepine antagonist in animals immobilized with high doses of TZ is not recommended. However, in combination with M, the effective dose of TZ can be reduced by as much as 50-75% (Onuma, 2003; Scandinavian Brown Bear Project, 2003; Arnemo et al., 2001; Caulkett et al., 1999; Cattet and Caulkett, 1997) Onuma in polar bears can be reduced by as much as 75%, and A can then be used to shorten the recoveries. The physiologic effects of MTZ have been studied in polar bears (Caulkett et al., 1997), black bears (Cattet and Caulkett, 1999), sun bears (Onuma, 2003), and brown bears (Arnemo et al., 2001; Scandinavian Brown Bear Project, 2003) and this drug combination is well tolerated by healthy individuals.^{2,3}

The mortality rate in the Scandinavian Brown Bear Project has been very low and only three animals (0.4%) have died during the 818 captures carried out so far. This shows that MTZ has a wide safety margin also in brown bears. However, studies on drug tolerance have not been performed. For obvious reasons, experimental trials with lethal doses cannot be done in free-ranging brown bears. In several zoos, however, surplus bears are euthanized as part of the parks management program. In the present study, we report experiments with excessive doses of MTZ in captive bears. In the first part of the study (carried out in Orsa Grönklitt), two bears were immobilized with a standard dose of MTZ and they were then repeatedly given iterations during a one hour period before termination by pentobarbital injections. In the second part of the study (carried out in Skånes Djurpark), three bears were given an excessive overdose (3-4 times the standard dose) initially followed by monitoring of physiologic effects. The results are summarized in Tables 1-5.

¹ M: Medetomidine (Domitor® 1 mg/ml, Zalopine® 10 mg/ml, Orion Pharma Animal Health, Turku, Finland)

² TZ: Tiletamine-Zolazepam (Zoletil® 500 mg/vial, Virbac, Carros, France)

³ A: Atipamezole (Antisedan® 5 mg/ml, Orion Pharma Animal Health, Turku, Finland)

Table 1. 2.5 year-old captive female (BM 120 kg)

Time	Drug & Dose	Comments
06.34	2 mg M + 500 mg TZ	Dart injection; animal in cage
06.36		Down
06.44	2 mg M + 500 mg TZ	Dart injection, animal in cage
		Transport to another facility
06.59	2 mg M	Hand syringe i.m.
07.04	2 mg M + 500 mg TZ	Dart injection (by hand)
07.09	2 mg M	Hand syringe i.m.
07.14	2 mg M	Hand syringe i.m.
07.19	2 mg M	Hand syringe i.m.
07.24	10 mg M	Hand syringe i.m.
07.39	150 ml Pentobarbital	Euthanized by i.v./i.c. administration
07.50		Respiratory and cardiac arrest

SUMMARY

Total dose: 24 mg M + 1500 mg TZ (0.2 mg M/kg + 12.5 mg TZ/kg)

Pulse oximetry (06.56-07.39): Mean = 93%; Max = 98%; Min = 85%

Table 2. 2.5 year old captive female (BM 105 kg); 14 August 2003

Time	Drug & Dose	Comments
07.45	5 mg M + 250 mg TZ	Dart injection
07.50		Down
07.55	5 mg M + 250 mg TZ	Dart injection
08.05	5 mg M + 250 mg TZ	Hand syringe i.m.
08.15	5 mg M + 250 mg TZ	Dart injection (by hand)
08.25	5 mg M + 250 mg TZ	Hand syringe i.m.
08.35	5 mg M + 250 mg TZ	Hand syringe i.m.
08.45	5 mg M + 250 mg TZ	Hand syringe i.m.
08.55	5 mg M + 250 mg TZ	Hand syringe i.m.
09.05	5 mg M + 250 mg TZ	Hand syringe i.m.
09.15	5 mg M + 250 mg TZ	Hand syringe i.m.
09.25	5 mg M + 250 mg TZ	Hand syringe i.m.
0930-09.33	100 ml Pentobarbital	Euthanized by i.v./i.c. administration
09.35		Respiratory and cardiac arrest

SUMMARY

Total dose: 55 mg M + 2750 mg TZ (0.52 mg M/kg + 26.2 mg TZ/kg)

Pulse oximetry (07.55-09.34): Means (4 periods) = 69, 70, 79, and 69 %, respectively.

Heart rate: 56-68 (significant sinus arrhythmia)

Respiratory rate: 4-6 breaths/min

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