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Physiological Effects of Medetomidine-Zolazepam-Tiletamine Immobilization in Black Bears

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ABSTRACT: A combination of medetomidine-zolazepam-tiletamine (MZT) was used to immobilize four black bears (Ursus americanus). The drugs were used at a dose of approximately 52 μg/kg of medetomidine, 0.86 mg/kg of zolazepam, and 0.86 mg/kg of tiletamine. Induction occurred in 6.3 ± 3.3 min (mean ± SD). The combination produced minimal adverse cardiopulmonary effects. Hypertension occurred in all four bears. Oxygenation and ventilation was good in three of the four bears. One bear demonstrated slight hypoxemia and hypoventilation at 15 min following drug administration. At one hr following drug administration atipamezole was administered at a dose of approximately 240 μg/kg. Recovery time was taken as the time from administration of the atipamezole until the time that the bear was sitting in the trap. Recovery occurred in 6.0 ± 4.1 min. MZT produced rapid, reliable immobilization in black bears with minimal adverse physiological effects. Immobilization, produced by this combination, was readily reversible with atipamezole.

Key words: Atipamezole, black bears, immobilization, medetomidine, reversible, tiletamine Ursus americanus, zolazepam.

Black bears (ursus americanus) frequently are immobilized for research or management purposes. In most situations it is desirable to use a drug combination that will produce rapid, reliable immobilization. It is often difficult to carry supportive equipment into the field; therefore, a drug combination that produces minimal adverse cardiopulmonary effects is important. Telazol® is a combination of tiletamine hydrochloride (HCl) and zolazepam HCl that has become popular for use in immobilization of bears (Haigh et al., 1985; Schobert, 1987; Taylor et al., 1989; Stirling et al., 1989; Gibeau and Paquet, 1991). One disadvantage of Telazol® is lack of a reversal agent. Some animals remain recumbent several hours post immobilization, making them a target for predation or subject to inclement weather. Medetomidine-ketamine is proving to be a promising combination in a variety of wildlife species. One major advantage of medetomidine-ketamine is the ability to reverse immobilization with atipamezole, a specific alpha-2 antagonist drug. Medetomidine-ketamine will probably prove to be a useful combination in a variety of species, but it does have some disadvantages. Hypertension and bradycardia often results following administration of medetomidine (Vainio et al., 1992; Caulkett et al., 1996a, 1996b). Bradycardia, produced by medetomidine, can result in decreased cardiac output (Vainio et al., 1992; Caulkett et al., 1996a). Hypoxemia has also been noted in several ruminant species (Jalanka, 1989; Caulkett et al., 1994, 1996b). Medetomidine-ketamine has been used in bears, but sudden recoveries have been reported (Jalanka and Roeken, 1990).

In order to address some of the above problems, we have developed a combination of medetomidine-zolazepam-tiletamine (MZT). This combination requires a lower dose of medetomidine than the medetomidine-ketamine combination, which should lead to decreased adverse effects from this drug. A relatively low dose of tiletamine and zolazepam is required, and antagonism of the medetomidine will result in arousal of the bear.

This study was performed in June 1996.
in the Meadow Lake region of central Saskatchewan (54°1' to 54°27'N, 109°11' to 109°25'W). Four black bears, one yearling male with an estimated weight of 50 kg, two sub-adult males with estimated weights of 60 and 70 kg, and one adult male with an estimated weight of 100 kg were used in this study. The bears were caught in culvert traps by officers of the Department of Environment and Resource Management (Loon Lake District Office and Meadow Lake Provincial Park, Saskatchewan, Canada). Traps were placed in a shaded area until the research team arrived. The weight of the bear was estimated to the nearest 10 kg. MZT was prepared by combining 2.5 mls of 6mg/ml medetomidine solution (Farmos Group, Turku, Finland) with zolazepam-tiletamine powder (Telazol®, Fort Dodge Laboratories, Inc, Fort Dodge, Iowa, USA) to produce a solution which contained 5.2 mg/ml of medetomidine, 86.2 mg/ml of tiletamine, and 86.2 mg/ml of zolazepam. MZT solution was administered into the muscles of the shoulder or the gluteal area via a 3 ml Telinject dart (Telinject GmbH, Ludwigshafen, Germany) projected with a blowpipe. The bears received medetomidine at a dose of approximately 52 µg/kg, tiletamine at a dose of approximately 0.86 mg/kg, and zolazepam at a dose of approximately 0.86 mg/kg. Induction time (IT) was defined as the time from drug administration to recumbency.

Once the bear was in sternal recumbency, it was removed from the trap and placed in dorsal recumbency. A 20 gauge, 5 cm catheter (Surflo, Terumo Medical Corp., Elkton, Maryland, USA) was placed in the femoral artery. Non-compliant tubing was used to connect the arterial catheter to a pressure transducer (Uniflow, Baxter Healthcare Corp., Irvine, California, USA), this was in turn connected to a physiological monitor (Propaq 400, Protocol Systems Inc., Beaverton, Oregon, USA). The transducer was zero calibrated midway between the spine and the scapula at approximately the sixth intercostal space. The monitor was used to measure direct systolic (SAP), mean (MAP) and diastolic (DAP) blood pressure, and heart rate (HR). Respiratory rate (RR) was determined by counting chest excursions over 1 min. Rectal temperature (RT) was measured using a temperature probe connected to the Propaq 400 monitor. Percent hemoglobin saturation (SaO2) was measured using a Nellcor Durasensor 100A probe (Nellcor Inc., Pleasanton, California, USA) connected to the Propaq 400 monitor. We recorded SAP, MAP, DAP, HR, RR, RT and SaO2 were recorded every 5 min from 15 to 60 min post immobilization. Arterial blood samples were withdrawn into heparinized syringes at 15, 30, 45 and 60 min post immobilization. These samples were placed in iced water and analyzed within 4 hr of sampling. Blood gas values were corrected for body temperature and hemoglobin concentration. Samples from three bears were used to determine pH, arterial carbon dioxide tension (PaCO2), arterial oxygen tension (PaO2) and base excess (BE). A lead II electrocardiograph (ECG) was observed continuously to monitor for arrhythmias.

At 60 min post immobilization the monitoring equipment was removed, and the bear was placed back into the culvert trap. Atipamezole was administered at a dose of approximately 240 µg/kg. One half of the dose was administered intravenously (IV) into the jugular vein, and half was administered intramuscularly (IM) into the muscles of the neck. Time to reversal of immobilization (RT) was taken as the time from administration of the atipamezole until the time that the bear was sitting in the trap. Immediately following recovery the bears were driven to a remote location and released.

Induction time averaged 6.3 ± 3.3 min (mean ± SD; range 1.5–9 min). The recovery time, following administration of atipamezole, was 6.0 ± 4.1 min (range 2–10 min). All bears were able to leave the trap and ambulate when they were re-
TABLE 1. Cardiopulmonary measurements (mean ± SD) in black bears immobilized for one hour with medetomidine-tiletamine-zolazepam.

<table>
<thead>
<tr>
<th></th>
<th>Time following drug administration</th>
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<tbody>
<tr>
<td></td>
<td>15 min</td>
</tr>
<tr>
<td>Heart rate (beats/min)(a)</td>
<td>61 ± 10</td>
</tr>
<tr>
<td>Resp. rate (breaths/min)(a)</td>
<td>11 ± 3</td>
</tr>
<tr>
<td>Mean art. press. (mmHg)(a)</td>
<td>211 ± 42</td>
</tr>
<tr>
<td>Rectal temperature (°C)(a)</td>
<td>37.5 ± 0.1</td>
</tr>
<tr>
<td>Hemoglobin saturation (%)*</td>
<td>90 ± 9</td>
</tr>
<tr>
<td>pH(b)</td>
<td>7.30 ± 0.03</td>
</tr>
<tr>
<td>PaCO2 (mmHg)(b,c)</td>
<td>43.3 ± 6.2</td>
</tr>
<tr>
<td>PaO2 (mmHg)(b,d)</td>
<td>68.5 ± 12.2</td>
</tr>
<tr>
<td>Base excess(b)</td>
<td>−4.0 ± 1.7</td>
</tr>
</tbody>
</table>

\(a\) \(n = 4\) bears.
\(b\) \(n = 3\) bears.
\(c\) Arterial carbon dioxide tension.
\(d\) Arterial oxygen tension.

Physiological measurements are listed in Table 1.

Immobilization with MZT was characterized by hypertension, and mild acidosis (Table 1). The authors could find no record of “normal” blood pressure in black bears, but a mean arterial pressure of approximately 90–100 mmHg is considered normal in humans and other unstressed mammals of a similar size. Mean arterial pressure in these bears was considerably higher than would be expected for an animal this size. Blood pressure tended to decrease over time. Hypertension is a common finding in animals immobilized with high doses of medetomidine (Vainio and Palmu 1989; Vainio et al. 1992; Caulkett et al. 1994), and is probably due to activation of peripheral alpha 2-adrenoceptors (Savola et al. 1986). Bradycardia is commonly encountered in animals immobilized with medetomidine-ketamine (Vainio and Palmu 1989; Jalkana and Roekien, 1990; Caulkett et al. 1994). Bears in this study maintained a heart rate of approximately 60 beats/min, this would probably not be considered to be a significant bradycardia in an animal of this size.

Oxygenation was good in these bears. Blood gas analysis was performed on three of the four bears, and pulse oximetry was performed on all four bears. However, one bear demonstrated hypoxemia (PaO2 < 60 mmHg), with a PaO2 of 56.6 mmHg at 15 min post immobilization. This bear improved over time and demonstrated a PaO2 of 67.3 mmHg at 60 min following drug administration. The hypoxemia experienced by this bear was transient and it probably was of little clinical significance. Ventilation was adequate throughout the immobilization with a mean PaCO2 of approximately 43 to 45 mmHg. The bear that developed hypoxemia also developed mild hypoventilation with a PaCO2 of 50.4 mm Hg at 15 min post immobilization. Hypoxemia and hypoventilation (Jalkana 1989; Caulkett et al. 1994, 1996b) have been observed in ruminants immobilized with medetomidine-ketamine. Mild acidosis was present in these bears, acidosis was most pronounced in the bear that experienced hypoventilation, and appears to be a respiratory acidosis. The lowest pH measured in this bear was 7.26, this would be well tolerated in a healthy animal. Body temperature tended to increase over time; however, the increase was relatively small (approximately 1°C). The ambient temperature was approximately 25°C during most of this study.

Induction of immobilization was rapid and smooth in all of these bears, muscle relaxation was good, and all bears re-
mained completely immobilized and unresponsive to stimuli throughout the immobilization period. Atipamezole was administered at a total dose of four times the medetomidine dose (weight/weight). Half of the dose was administered IV and half of the dose was administered IM. The IV fraction of the dose was administered to produce a rapid recovery. The IM fraction should be absorbed “slower” and outlast the effects of the medetomidine. The authors have used this route of administration in previous studies and have not noted remarcotization. Jalanka (Jalanka 1993) recommended that ruminants, immobilized with medetomidine-ketamine, should receive atipamezole at four times the medetomidine dose, with half administered IV or IM and half administered by subcutaneous injection (SC). Jalanka (1993) recommended that carnivores receive atipamezole at 2–3 times the medetomidine dose IM or SC, to antagonize medetomidine-ketamine induced immobilization. The percentage of ketamine in medetomidine-ketamine combinations for use in carnivores is higher than that used in ruminants (Jalanka, 1993). Complete reversal of the medetomidine with IV of high IM doses of atipamezole can result in ataxic recoveries or overalertness in carnivores (Jalanka, 1993). With MZT it is possible to “fully antagonize” the medetomidine as the zolazepam in the mixture will still modulate the effects of the tiletamine. Recovery was rapid, although bears appeared to be somewhat disoriented on recovery and they were probably experiencing some residual effects of the zolazepam and tiletamine. All bears were able to vacate the trap and ambulate within 1 hr post reversal.

Cardiopulmonary effects of this combination were minimal, particularly since these are relatively large animals that were maintained in dorsal recumbency, without supplemental oxygen. This was a preliminary study, with a small sample size. Further studies are required to characterize the efficacy and safety of this combination in black bears and other species.

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LITERATURE CITED


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