

## EFFICACY OF A PORTABLE OXYGEN CONCENTRATOR WITH PULSED DELIVERY FOR TREATMENT OF HYPOXEMIA DURING ANESTHESIA OF WILDLIFE

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**Abstract:** Portable battery-driven oxygen concentrators provide an alternative to the use of oxygen cylinders for treatment of hypoxemia during field anesthesia. The aim of this study was to evaluate the use of the EverGo™ Portable Oxygen Concentrator (Respironics®, Murrysville, Pennsylvania 15668, USA) with pulse-dose delivery for improvement of arterial oxygenation during anesthesia of wildlife. This concentrator delivers oxygen in a pulsed flow with pulse volumes from 12 to 70 ml, up to a maximum capacity of 1.05 L/min. The pulse-dose setting shall be adjusted according to the respiratory rate of the animal, e.g., setting 6 for a respiratory rate  $\leq 15$ /min. The study included 16 free-ranging brown bears (*Ursus arctos*), 18 free-ranging bighorn sheep (*Ovis canadensis*), and five captive reindeer (*Rangifer tarandus*). Oxygen was administered via two nasal lines that were inserted through the nostrils to the level of the medial canthus of the eyes. Arterial blood samples were collected before, during, and after oxygen therapy and immediately analyzed. When providing oxygen from the portable concentrator, the arterial oxygenation markedly improved in all brown bears and some reindeer, whereas no or minor improvement was seen in the bighorn sheep. The mean  $\pm$  SD (range) PaO<sub>2</sub> during oxygen supplementation was  $134 \pm 29$  (90–185) mmHg in the brown bears,  $52 \pm 11$  (32–67) mmHg in the bighorn sheep, and  $79 \pm 19$  (61–110) mmHg in the reindeer. The efficacy of the evaluated method may be influenced by ambient temperature, altitude, pulse-dose setting on the concentrator, the animal's respiratory rate, and species-specific physiology during anesthesia. Advantages of the portable oxygen concentrator included small size and low weight, ease of operate, and rechargeability.

**Key words:** Anesthesia, hypoxemia, immobilization, oxygen concentrator, oxygen therapy, wildlife.

### INTRODUCTION

Hypoxemia commonly develops during anesthesia of many wildlife species.<sup>12,14,21</sup> Although hypoxemia can lead to morbidity as well as mortality during and after anesthesia, it is not always treated, or even detected. Pulse oximeters may indicate hypoxemia, but are not always accurate.<sup>12,14</sup> Arterial blood gas analysis is per-

formed to detect the presence and severity of hypoxemia. Blood gas analysis is considered gold standard for measurement of arterial oxygenation, but might not be feasible in the field at all times. If accurate assessment of oxygenation is not available, oxygen supplementation should be provided as part of standard procedure when anesthetizing wildlife.

For oxygen therapy in the field, lightweight cylinders with compressed oxygen are easy to carry, but they require complex logistics to refill during remote fieldwork. In addition, compressed oxygen cylinders can be explosive under certain circumstances, and there are restrictions for transportation aboard aircraft, including helicopters. An alternative to oxygen cylinders is portable battery-driven oxygen concentrators, which are widely used in industrial countries for home treatment of people and for travel applications.<sup>9</sup> In developing countries, where oxygen cylinders pose considerable logistics and financial problems, oxygen concentrators are successfully being used in human hospitals and field situations.<sup>11,22</sup>

Portable oxygen concentrators work by molecular sieve technology.<sup>15</sup> Ambient air is filtered, compressed, and then passed alternately through

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two canisters of zeolite, which is a silicate compound that adsorbs nitrogen from the air and concentrates oxygen up to 96%. Depending on the model, the presently available portable oxygen concentrators can provide oxygen by continuous flow up to 3 L/min, by pulse-dose delivery, or both. With continuous-flow oxygen therapy, only a portion of the oxygen delivered reaches the alveoli of the patient, because oxygen provided during exhalation is wasted. Pulse-dose oxygen delivery (demand oxygen delivery) is triggered by the patient's inspiration and delivers oxygen on demand during the inspiratory phase, which is the most important time for participation in gas exchange in the lungs. Some portable oxygen concentrators deliver a constant pulse volume of oxygen, independent of respiratory rate (fixed pulse volume). Other concentrators deliver a constant volume of oxygen per minute (fixed oxygen minute volume), so the pulse volume per breath decreases as respiratory rate increases.<sup>9</sup>

The hypothesis was that a portable battery-driven oxygen concentrator would be an efficient oxygen delivery device for treatment of hypoxemia during field anesthesia of wild animals. To the best of our knowledge, portable concentrators have not yet been evaluated for use in either domestic or wild animals. The aim of this study was to evaluate the efficacy of a portable oxygen concentrator with pulse-dose delivery for improvement of arterial oxygenation during anesthesia of wildlife.

## MATERIALS AND METHODS

### Animals, study areas, drugs, and capture methods

**Brown bears (*Ursus arctos*):** Sixteen free-ranging brown bears (6 adults, 3 subadults, 7 yearlings) with body mass ranging between 13 and 228 kg were included in the study (Table 1). The animals were darted from a helicopter in April 2009 and 2010, in the county of Dalarna, Sweden. Capture took place at altitudes ranging between 200 and 700 m (barometric pressure [ $P_B$ ] 707–743 mmHg, ambient temperature 5–16°C). The animals were anesthetized for radiomarking for ecological studies within the Scandinavian Brown Bear Research Project. For anesthesia, medetomidine hydrochloride (HCl) (Domitor<sup>®</sup> vet., 1 mg/ml, or Zolopine, 10 mg/ml, Orion Pharma Animal Health, FI-02200 Espoo, Finland) at 0.04–0.13 mg/kg was used in combination with zolazepam and tiletamine (Zoletil forte vet., Virbac S.A., 06510 Carros, France) at 2.1–6.4

mg/kg. The capture procedure and physiologic evaluation of anesthesia with this drug combination in brown bears have been described in detail.<sup>12,13</sup> The brown bears had surgery for placement of intraperitoneal radiotransmitters and for analgesia 4 mg/kg carprofen (Rimadyl<sup>®</sup> vet. 50 mg/ml, Orion Pharma Animal Health, FI-02200 Espoo, Finland) was administered subcutaneously before surgery. Approval was given by the Ethical Committee on Animal Experiments in Uppsala, Sweden.

**Bighorn sheep (*Ovis canadensis*):** Eighteen free-ranging bighorn sheep (2 adults, 6 yearlings, 10 lambs) with body mass ranging between 22 and 79 kg were included in the study (Table 2). The animals were anesthetized for ear tagging as part of an ongoing long-term study on the ecology and behavior of bighorn sheep. Fifteen capture events took place in the Sheep River Provincial Park (altitude 1,460–1,640 m,  $P_B$  609–640 mmHg, ambient temperature 1–12°C) and three in the Highwood area (altitude 2,105–2,230 m,  $P_B$  575–591 mmHg, ambient temperature 6–22°C) in Kananaskis Country, Alberta, Canada, between September and December 2009 and 2010. For initial darting, medetomidine HCl (Medetomidine 30 mg/ml, Bow Valley Research Inc., Calgary, Alberta T2N 4G3, Canada) at 0.08–0.21 mg/kg was used in combination with ketamine HCl (Vetalar, 100 mg/ml, Bioniche, Animal Health Canada, Inc., Belleville, Ontario K8N 5J2, Canada) at 1.5–5.1 mg/kg. In seven animals, which required a second dart or additional drug injection by hand, total doses up to 0.31 mg/kg medetomidine and 10.2 mg/kg ketamine were administered. The animals were darted in the hindquarter from a distance of 10–15 m by firing a dart rifle (Telinject U.S.A., Inc., Agua Duce, California 91390, USA, or Dan-Inject Injection Rifle model JM Special, Dan-Inject, DK-7080 Børkop, Denmark) from a vehicle ( $n = 7$ ) or on foot ( $n = 11$ ). For darting, 1.5- or 3-ml dart syringes with collared or barbed needles (1.5 × 20 mm, 1.5 × 25 mm, 2 × 30 mm, or 2 × 40 mm) were used. Once recumbent, the sheep were positioned in sternal recumbency with head up and nose down, but during blood collection from the femoral artery, the hindquarters of the animals were positioned lateral.

**Reindeer (*Rangifer tarandus*):** Five captive reindeer (2 adults, 3 yearlings) with body mass ranging between 100 and 150 kg were included in the study (Table 3). The animals were anesthetized for antler removal at the Wildlife Research Station on Spyhills Campus (1,278 m,  $P_B$  676

**Table 1.** Effects of intranasal oxygen supplemented from a portable oxygen concentrator with pulsed delivery during medetomidine–zolazepam–tiletamine anesthesia of 14 free-ranging brown bears. The goal was to improve the animals' arterial oxygenation to reach a target PaO<sub>2</sub> of 83 mmHg, which was calculated as the expected value in a normal awake animal at the present altitude in Dalarna, Sweden.<sup>a</sup>

Age and sex	Body mass (kg)	O <sub>2</sub> concentrator setting	Pre-O <sub>2</sub> and minutes of O <sub>2</sub> supplementation	RR (bpm)	PaO <sub>2</sub> <sup>b</sup> (mmHg)	Actual PaO <sub>2</sub> – target PaO <sub>2</sub>	SaO <sub>2</sub> (%)	SpO <sub>2</sub> (%)	PaCO <sub>2</sub> <sup>b</sup> (mmHg)
Adult male	209	–	Pre-O <sub>2</sub>	12	65	–18	86	91	35
		<b>6</b>	<b>17</b>	<b>8</b>	<b>96</b>	<b>+13</b>	<b>95</b>	<b>95</b>	<b>39</b>
Adult male	183	–	Pre-O <sub>2</sub>	8	58	–25	81	NR	50
		<b>6</b>	<b>44</b>	<b>20</b>	<b>90</b>	<b>+7</b>	<b>95</b>	<b>NR</b>	<b>54</b>
Adult male	98	–	Pre-O <sub>2</sub>	16	74	–9	91	NW	44
		<b>6</b>	<b>11</b>	<b>16</b>	<b>118</b>	<b>+35</b>	<b>98</b>	<b>93</b>	<b>42</b>
Adult female	97	–	Pre-O <sub>2</sub>	13	76	–7	90	86	44
		<b>6</b>	<b>16</b>	<b>10</b>	<b>110</b>	<b>+27</b>	<b>97</b>	<b>91</b>	<b>47</b>
Subadult female	59	–	Pre-O <sub>2</sub>	15	67	–16	86	NR	43
		<b>5.5</b>	<b>15</b>	<b>12</b>	<b>116</b>	<b>+33</b>	<b>97</b>	<b>NW</b>	<b>47</b>
Subadult male	55	–	Pre-O <sub>2</sub>	5	70	–13	88	92	41
		<b>6</b>	<b>10</b>	<b>5</b>	<b>128</b>	<b>+45</b>	<b>98</b>	<b>84</b>	<b>47</b>
Subadult male	27	–	Pre-O <sub>2</sub>	7	49	–34	75	NW	50
		<b>6</b>	<b>20</b>	<b>7</b>	<b>133</b>	<b>+50</b>	<b>98</b>	<b>96</b>	<b>50</b>
Yearling male	27	–	Pre-O <sub>2</sub>	18	93	+10	93	92	36
		<b>3</b>	<b>25</b>	<b>10</b>	<b>125</b>	<b>+42</b>	<b>98</b>	<b>97</b>	<b>44</b>
Yearling male	25	–	Pre-O <sub>2</sub>	12	71	–12	87	81	44
		<b>3</b>	<b>15</b>	<b>16</b>	<b>131</b>	<b>+48</b>	<b>98</b>	<b>87</b>	<b>50</b>
Yearling male	24	–	Pre-O <sub>2</sub>	14	70	–13	90	89	36
		<b>3</b>	<b>13</b>	<b>20</b>	<b>144</b>	<b>+61</b>	<b>99</b>	<b>86</b>	<b>42</b>
Yearling male	20	–	Pre-O <sub>2</sub>	5	68	–15	90	NR	37
		<b>6</b>	<b>15</b>	<b>5</b>	<b>155</b>	<b>+72</b>	<b>99</b>	<b>NR</b>	<b>43</b>
Yearling male	18	–	Pre-O <sub>2</sub>	17	84	+1	95	NW	33
		<b>5</b>	<b>20</b>	<b>30</b>	<b>185</b>	<b>+102</b>	<b>100</b>	<b>NW</b>	<b>42</b>
Yearling female	17	–	Pre-O <sub>2</sub>	15	83	0	90	NR	32
		<b>6</b>	<b>15</b>	<b>12</b>	<b>175</b>	<b>+92</b>	<b>99</b>	<b>NR</b>	<b>39</b>
Yearling male	13	–	Pre-O <sub>2</sub>	16	89	+6	94	73	39
		<b>3</b>	<b>15</b>	<b>16</b>	<b>171</b>	<b>+88</b>	<b>99</b>	<b>90</b>	<b>49</b>

<sup>a</sup> RR = respiratory rate; bpm = breaths/min; SpO<sub>2</sub> = hemoglobin oxygen saturation measured by pulse oximetry; NR = not recorded due to ongoing procedures in the field; NW = not working, i.e., the pulse oximeter failed to produce a reading; SaO<sub>2</sub> = arterial hemoglobin oxygen saturation (calculated value); PaO<sub>2</sub> and PaCO<sub>2</sub> = partial pressures of arterial oxygen and carbon dioxide (measured values). Blood gas values were corrected to the rectal temperature (range 37.5–41.1°C). Boldface indicates values during oxygen supplementation from the portable oxygen concentrator.

<sup>b</sup> Increased significantly following oxygen supplementation ( $P < 0.05$ ).

mmHg, ambient temperature 24°C), Faculty of Veterinary Medicine, University of Calgary, Canada in August 2009. For anesthesia, detomidine HCl (Dormosedan, 10 mg/ml, Pfizer Animal Health, Pfizer Canada Inc., Kirkland, Québec H9J 2M5, Canada) at 0.14–0.28 mg/kg was used in combination with ketamine HCl (Vetalar, 100 mg/ml, Bioniche) at 2.8–6.0 mg/kg and hydro-morphine HCl (Hydromorphone, 100 mg/ml, Sabex Inc., Boucherville, Québec J4B 7K8, Canada) at 0.2–0.3 mg/kg. The animals were darted in the hindquarter while in a pen within a handling facility. For darting, 3-ml dart syringes with 2.0 × 40-mm barbed needles were fired from a CO<sub>2</sub> powered rifle (Dan-Inject). Once recumbent, the

reindeer were positioned in lateral recumbency. Approval for the reindeer and bighorn sheep studies was given by the Animal Care Committee at University of Calgary, Canada.

For reversal of the effects of medetomidine in brown bears and bighorn sheep, atipamezole HCl (Atipamezole, 20 mg/ml, Bow Valley Research, or Antisedan<sup>®</sup>, 5 mg/ml, Pfizer Animal Health) was administered intramuscularly (i.m.) at five times the medetomidine dose. For anesthetic reversal in reindeer, tolazoline HCl (Tolazoline 100 mg/ml, Bow Valley Research) was administered half i.m. and half intravenously (i.v.), at a total dose of 300–950 mg (3–4 mg/kg), atipamezole (Antisedan<sup>®</sup>, 5 mg/ml, Pfizer Animal Health) i.m. at a total dose

**Table 2.** Effects of intranasal oxygen supplemented from a portable oxygen concentrator or an oxygen cylinder (in italics) during medetomidine–ketamine anesthesia of 18 free-ranging bighorn sheep. The goal was to improve the animals' arterial oxygenation to reach a target PaO<sub>2</sub> of 73 mmHg in Sheep River (SR) and 62 mmHg in Highwood (H), which was calculated as the expected value in a normal awake animal at the present altitude in Canada.<sup>a</sup>

Age and sex	Body mass (kg)	Location	O <sub>2</sub> concentrator setting	O <sub>2</sub> cylinder flow rate (L/min)	Pre-O <sub>2</sub> and minutes of O <sub>2</sub> supplementation	RR (breaths/min)	PaO <sub>2</sub> <sup>b</sup> (mmHg)	Actual PaO <sub>2</sub> – target PaO <sub>2</sub>	PaCO <sub>2</sub> <sup>b</sup> (mmHg)
Adult female	79	H	–	–	Pre-O <sub>2</sub>	92	40	–22	54
			<b>1</b>	–	<b>20</b>	<b>96</b>	<b>30</b>	<b>–32</b>	<b>52</b>
Adult female	57	H	–	–	Pre-O <sub>2</sub>	96	28	–34	50
			<b>6</b>	–	<b>14</b>	<b>112</b>	<b>32</b>	<b>–30</b>	<b>53</b>
Yearling female	62	SR	–	–	Pre-O <sub>2</sub>	100	50	–23	55
			<b>6</b>	–	<b>20</b>	<b>88</b>	<b>57</b>	<b>–16</b>	<b>58</b>
Yearling female	55	SR	–	<b>6</b>	<b>12, O<sub>2</sub> cylinder</b>	<b>84</b>	<b>89</b>	<b>+16</b>	<b>63</b>
			–	–	Pre-O <sub>2</sub>	90	36	–37	53
			<b>6</b>	–	<b>10</b>	<b>83</b>	<b>45</b>	<b>–28</b>	<b>56</b>
Yearling female	54	SR	–	<b>6</b>	<b>37, O<sub>2</sub> cylinder</b>	<b>92</b>	<b>68</b>	<b>–5</b>	<b>66</b>
			–	–	Pre-O <sub>2</sub>	55	35	–38	52
Yearling male	54	SR	–	–	Pre-O <sub>2</sub>	55	35	–38	52
			<b>1</b>	–	<b>39</b>	<b>80</b>	<b>34</b>	<b>–39</b>	<b>57</b>
Yearling female	53	SR	–	–	Pre-O <sub>2</sub>	36	52	–21	51
			<b>3</b>	–	<b>22</b>	<b>66</b>	<b>45</b>	<b>–28</b>	<b>60</b>
Yearling female	43	SR	–	–	Pre-O <sub>2</sub>	101	32	–41	62
			<b>1</b>	–	<b>14</b>	<b>84</b>	<b>25</b>	<b>–48</b>	<b>63</b>
Yearling female	42	SR	–	–	Pre-O <sub>2</sub>	120	42	–31	53
			<b>1</b>	–	<b>20</b>	<b>104</b>	<b>48</b>	<b>–25</b>	<b>53</b>
Lamb female	38	SR	–	–	Pre-O <sub>2</sub>	24	53	–20	53
			<b>3.5–2</b>	–	<b>16</b>	<b>35</b>	<b>91</b>	<b>+18</b>	<b>62</b>
Lamb male	36	H	–	–	Pre-O <sub>2</sub>	75	47	–15	47
			<b>1</b>	–	<b>22</b>	<b>56</b>	<b>67</b>	<b>+5</b>	<b>55</b>
Lamb male	34	SR	–	–	Pre-O <sub>2</sub>	72	36	–37	57
			<b>6</b>	–	<b>23</b>	<b>124</b>	<b>39</b>	<b>–34</b>	<b>52</b>
Lamb male	35	SR	–	–	Pre-O <sub>2</sub>	100	55	–18	53
			<b>1</b>	–	<b>34</b>	<b>116</b>	<b>56</b>	<b>–17</b>	<b>52</b>
Lamb female	33	SR	–	–	Pre-O <sub>2</sub>	92	44	–29	59
			<b>1</b>	–	<b>24</b>	<b>96</b>	<b>55</b>	<b>–18</b>	<b>58</b>
Lamb male	32	SR	–	–	Pre-O <sub>2</sub>	122	35	–38	59
			<b>6</b>	–	<b>13</b>	<b>122</b>	<b>32</b>	<b>–41</b>	<b>55</b>
Lamb female	31	SR	–	–	Pre-O <sub>2</sub>	92	28	–45	66
			<b>1</b>	–	<b>21</b>	<b>70</b>	<b>60</b>	<b>–13</b>	<b>72</b>
Lamb female	30	SR	–	–	Pre-O <sub>2</sub>	73	28	–45	58
			<b>1.5–1</b>	–	<b>10</b>	<b>119</b>	<b>50</b>	<b>–23</b>	<b>63</b>
Lamb male	26	SR	–	–	Pre-O <sub>2</sub>	128	38	–35	59
			<b>1</b>	–	<b>20</b>	<b>120</b>	<b>37</b>	<b>–36</b>	<b>61</b>
Lamb male	22	SR	–	–	Pre-O <sub>2</sub>	80	36	–37	52
			<b>1</b>	–	<b>22</b>	<b>94</b>	<b>55</b>	<b>–18</b>	<b>52</b>

<sup>a</sup> RR = respiratory rate; PaO<sub>2</sub> and PaCO<sub>2</sub> = partial pressures of arterial oxygen and carbon dioxide (measured values). Blood gas values were corrected to the rectal temperature (range 37.0–40.8°C). Boldface indicates values during oxygen supplementation from the portable oxygen concentrator and boldface italics indicates supplementation from an oxygen cylinder.

<sup>b</sup> Increased significantly following oxygen supplementation ( $P < 0.05$ ).

of 12–20 mg (0.1–0.2 mg/kg), and naloxone HCl (Narcan, 0.4 mg/ml, Sabex) half i.m. and half i.v. at a total dose of 2–3 mg.

### Blood sampling and analysis

Arterial blood samples were collected anaerobically before (pre-O<sub>2</sub>) and during oxygen supple-

mentation from all animals. In the captive setting, arterial samples were collected from reindeer within 6–9 min of starting the oxygen supplementation. During anesthesia of free-ranging brown bears and bighorn sheep, the goal was to collect arterial samples within 10–25 min of starting the oxygen supplementation. Samples were collected

**Table 3.** Effects of intranasal oxygen supplemented from a portable oxygen concentrator during detomidine-ketamine anesthesia of captive reindeer in Calgary, Canada. The goal was to improve the animals' arterial oxygenation to reach a target PaO<sub>2</sub> of 82 mmHg, which was calculated as the expected value in a normal awake animal at the present altitude.<sup>a</sup>

Age and sex	Body mass (kg)	O <sub>2</sub> concentrator setting	Pre-O <sub>2</sub> and minutes of O <sub>2</sub> supplementation	RR (breaths/min)	PaO <sub>2</sub> (mmHg)	Actual PaO <sub>2</sub> – target PaO <sub>2</sub>	PaCO <sub>2</sub> (mmHg)
Adult male <sup>b</sup>	150 (est.)	–	Pre-O <sub>2</sub>	20	56	–26	42
		<b>6</b>	<b>7</b>	<b>28</b>	<b>68</b>	<b>–14</b>	<b>57</b>
Adult male	145	–	Pre-O <sub>2</sub>	32	32	–50	41
		<b>6</b>	<b>9</b>	<b>40</b>	<b>78</b>	<b>–4</b>	<b>34</b>
Yearling male	120	–	Pre-O <sub>2</sub>	20	55	–27	39
		<b>6</b>	<b>6</b>	<b>16</b>	<b>61</b>	<b>–21</b>	<b>45</b>
Yearling male <sup>c</sup>	110 (est.)	–	Pre-O <sub>2</sub>	12	55	–27	42
		<b>6</b>	<b>7</b>	<b>15</b>	<b>61</b>	<b>–21</b>	<b>45</b>
Yearling male	100 (est.)	–	Pre-O <sub>2</sub>	24	31	–51	50
		<b>6</b>	<b>6</b>	<b>20</b>	<b>110</b>	<b>+28</b>	<b>43</b>

<sup>a</sup> RR = respiratory rate; PaO<sub>2</sub> and PaCO<sub>2</sub> = partial pressures of arterial oxygen and carbon dioxide (measured values). Blood gas values were corrected to the rectal temperature (range 38.1–41.5°C). Boldface indicates values during oxygen supplementation. (est.) = estimated body mass.

<sup>b</sup> Nasal lines may have been dislodged from the nares briefly when antlers were removed.

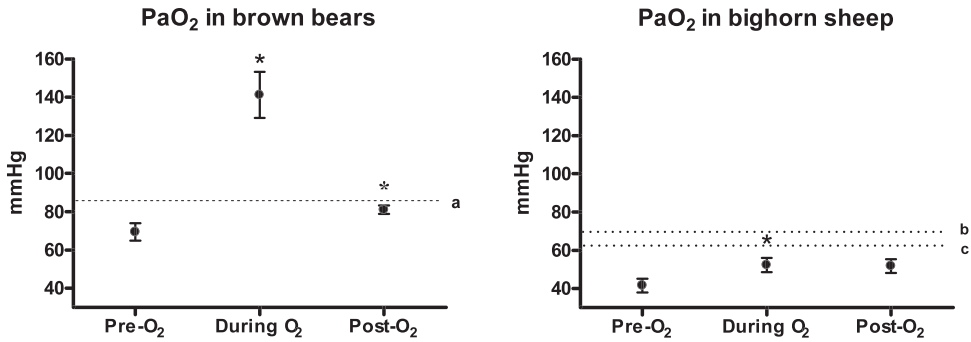
<sup>c</sup> Nasal lines were blocked with secretions, so oxygen was not delivered properly.

later in one brown bear because of ongoing procedures in the field and from two bighorn sheep because of difficulties in obtaining arterial blood. Arterial blood samples were also collected approximately 10 min after oxygen supplementation was discontinued (post-O<sub>2</sub>) in seven brown bears and eight bighorn sheep. In brown bears and reindeer, the samples were collected from the femoral artery. In bighorn sheep, the samples were collected from either the femoral or an auricular artery. Arterial flow was confirmed by using either self-filling syringes (PICO™70, Radiometer Copenhagen, Brønshøj, Denmark) or pulsed flow from open needle stick. Firm pressure was applied at the sample site for 2 min postsampling to avoid development of a hematoma. The samples were collected in preheparinized syringes, capped, and processed immediately with the use of a portable analyzer and cartridges (i-STAT®1 Portable Clinical Analyzer and i-STAT® cartridges CG4+, Abbott Laboratories, Abbott Park, Illinois 60064-6048, USA). The analysis included measured values for partial pressures of arterial oxygen (PaO<sub>2</sub>) and carbon dioxide (PaCO<sub>2</sub>). Calculated values for arterial hemoglobin oxygen saturation (SaO<sub>2</sub>) are presented for brown bears. Blood-gas values were corrected to the rectal temperature. Respiratory rate and rectal temperature were recorded at the time of arterial sampling. Heart rate, capillary refill time, muscle relaxation, and palpebral reflex were also monitored, but not presented here. In brown bears, hemoglobin oxygen saturation (SpO<sub>2</sub>) was monitored by pulse

oximetry, with the pulse oximeter probe attached to the tongue (Nellcor NBP-40 or N-20 Handheld Pulse Oximeter, Nellcor Inc., Pleasanton, California 94588, USA). Pulse oximetry data were not collected from bighorn sheep and reindeer because of difficulties in obtaining reliable readings from the pulse oximeter during anesthesia with the drug combinations used in the species.

### Oxygen concentrator and intranasal oxygen therapy

Intranasal oxygen supplementation was administered through pulsed delivery from a battery-driven oxygen concentrator (EverGo™ Portable Oxygen Concentrator, Respiroics®, Murrysville, Pennsylvania 15668, USA). This unit measures 30.5 × 15.2 × 21.6 cm and weighs 4.5 kg with two rechargeable batteries, which provide power for up to 8 hr depending on the setting. An oxygen concentration of approximately 90% is provided in the recommended operating conditions between 5 and 40°C, 15–95% relative humidity, and up to 2,438-m altitude. After startup, the unit requires ~10 min to reach its specified purity of oxygen. The concentrator delivers oxygen in a pulsed flow with pulse volumes from 12 to 70 ml, up to a maximum capacity of 1.05 L/min. Pulse-dose settings used in the different animals are presented in Tables 1–3. Two nasal lines with a 3-mm outside diameter were inserted through the nostrils into the nasal cavity to the level of the medial canthus of the eye. Initially the nasal lines were not secured in place, but in order to prevent



**Fig. 1.** Partial pressure of oxygen (PaO<sub>2</sub>, mean ± SD) in brown bears (*n* = 7) and bighorn sheep (*n* = 8) pre-, during and post-O<sub>2</sub> supplementation from a portable oxygen concentrator with pulse-dose delivery. The dotted lines represent target PaO<sub>2</sub> in Dalarna (a), Sweden, and in Sheep River Provincial Park (b) and Highwood (c), Canada. The asterisk indicates a significant difference (*P* < 0.05) from the previous sample.

dislodgement from the nares, procedures were changed to secure them in place with tape around the muzzle of bighorn sheep, and by towel clamps attached to the bridge of the nose of brown bears. Two bighorn sheep received intranasal oxygen delivered from an oxygen cylinder at a flow rate of 6 L/min, to determine if hypoxemia could be treated by a higher flow of supplemental oxygen.

The minimum goal with oxygen supplementation was to improve the animal's arterial oxygenation to reach a target PaO<sub>2</sub> that could be expected in a normal awake animal at the altitude of each capture area. The alveolar oxygen tension (PAO<sub>2</sub>) was calculated based on the alveolar gas equation [PAO<sub>2</sub> = F<sub>i</sub>O<sub>2</sub> (P<sub>B</sub> - P<sub>H<sub>2</sub>O</sub>) - (PaCO<sub>2</sub>/RQ)]. F<sub>i</sub>O<sub>2</sub> = fraction of inspired oxygen (0.21). P<sub>H<sub>2</sub>O</sub> = saturated vapor pressure for water at 37°C (47 mmHg). Local mean barometric pressure (P<sub>B</sub>) was used, and the respiratory quotient (RQ) was assumed to be 1 for bighorn sheep and reindeer, and 0.8 for brown bears. An assumed PaCO<sub>2</sub> of 35 mmHg was used, as reported in awake standing sheep at ~1,500-m elevation.<sup>16</sup> Assuming a normal alveolar-arterial oxygen tension difference [P(A-a)O<sub>2</sub>] of 15 mmHg,<sup>10</sup> the target PaO<sub>2</sub> was calculated by subtracting 15 from the calculated PAO<sub>2</sub> value. The resulting target PaO<sub>2</sub> for bighorn sheep was 73 mmHg in Sheep River and 62 mmHg in Highwood, Canada, 82 mmHg for captive reindeer in Calgary, Canada, and 83 mmHg for brown bears in Dalarna, Sweden. Animals were considered hypoxemic if their PaO<sub>2</sub> was below the calculated target value for each species and capture location.

#### Statistical analysis

The PaO<sub>2</sub> and PaCO<sub>2</sub> values and respiratory rate before and during oxygen supplementation

were compared with a paired two-tailed *t*-test. In animals where PaO<sub>2</sub> data were available pre-, during, and post-O<sub>2</sub>, a one-way repeated measures analysis of variance (ANOVA) followed by a post hoc Bonferroni's multiple comparison test were used to compare changes in oxygenation over time. GraphPad Prism (GraphPad Software, Inc., La Jolla, California 92037, USA) was used for all analyses. A *P* value < 0.05 was considered significant. Data are presented as mean ± SD (range). Blood gas data during oxygen supplementation from two brown bears and two reindeer were excluded from statistical analysis because the nasal lines became plugged with secretions, were dislodged from the nares, or became kinked or disconnected from the concentrator, so oxygen was not delivered properly.

## RESULTS

Arterial oxygenation markedly improved in most brown bears and reindeer during oxygen supplementation from the portable concentrator evaluated in this study (Tables 1 and 3). In contrast, no or minor improvement in PaO<sub>2</sub> was seen in the bighorn sheep (Table 2).

All but three brown bears were hypoxemic with pre-O<sub>2</sub> values of PaO<sub>2</sub> of 73 ± 11 (49–93) mmHg, *n* = 16. Following supplementation by the oxygen concentrator, the PaO<sub>2</sub> increased significantly to 134 ± 29 (90–185) mmHg, *n* = 14 (Table 1). The target PaO<sub>2</sub> of 83 mmHg was reached in all 14 brown bears to which oxygen supplementation was successfully delivered. The PaCO<sub>2</sub> increased significantly from 40 ± 6 (32–50) mmHg to 45 ± 4 (39–54) mmHg following oxygen supplementation, but it decreased or did not change in 2 of 12 brown bears (Table 1). A mild hypercapnia (PaCO<sub>2</sub> ≥ 45 mmHg) was recorded pre-O<sub>2</sub> in

two animals and during oxygen supplementation in seven animals (Table 1). There were seven brown bears from which pre-, during, and post-O<sub>2</sub> values of PaO<sub>2</sub> were available (Fig. 1). In these seven bears, the PaO<sub>2</sub> increased significantly during oxygen supplementation and decreased following discontinuation of oxygen to values that were not significantly different than pre-O<sub>2</sub> values.

All 18 bighorn sheep developed marked hypoxemia with pre-O<sub>2</sub> values of PaO<sub>2</sub> of  $40 \pm 9$  (28–55) mmHg. The P(A–a)O<sub>2</sub> was  $37 \pm 6$  (28–48) mmHg, calculated based on standard temperature, before oxygen supplementation was started. Following supplementation by the oxygen concentrator, the PaO<sub>2</sub> increased significantly to  $52 \pm 11$  (32–67) mmHg, but it decreased in 7 of 18 sheep, and all but 2 sheep remained hypoxemic (Table 2). The target PaO<sub>2</sub> was reached in 1 of 3 bighorn sheep anesthetized in the Highwood area and in 1 of 16 bighorn sheep in the Sheep River Provincial Park during oxygen supplementation from the concentrator (Table 2). One of the two bighorn sheep that were supplemented with oxygen from a cylinder reached the target PaO<sub>2</sub> (Fig. 1). The PaCO<sub>2</sub> increased significantly from  $55 \pm 5$  (47–66) mmHg to  $57 \pm 5$  (52–72) mmHg following oxygen supplementation, but it decreased in 7 of the 18 sheep (Table 2). Pre-, during, and post-O<sub>2</sub> values of PaO<sub>2</sub> were available in eight bighorn sheep (Fig. 1). In these eight animals, the PaO<sub>2</sub> increased significantly during oxygen supplementation. There was no significant decrease following discontinuation of oxygen. Side effects recorded during anesthesia of bighorn sheep included hypoxemia, hypercapnia, tachypnea, hyperthermia, salivation, and bloating, especially if in lateral recumbency. Bloating did not occur in reindeer although they were laterally recumbent throughout anesthesia.

All five reindeer developed marked hypoxemia with pre-O<sub>2</sub> values of PaO<sub>2</sub> of  $45 \pm 13$  (31–56) mmHg. Following supplementation by the oxygen concentrator, the PaO<sub>2</sub> was  $79 \pm 19$  (61–110) mmHg. The target PaO<sub>2</sub> of 82 mmHg was reached in one of three reindeer that oxygen supplementation was successfully delivered to from the portable concentrator (Table 3).

## DISCUSSION

This is the first study evaluating the use of a portable oxygen concentrator in animals, as one device was used during anesthesia of various wildlife species in the field. Following pulse-dose delivery of intranasal oxygen from the investigated concentrator, the arterial oxygenation marked-

ly improved in most brown bears and reindeer, whereas no or minor improvement was seen in the bighorn sheep. Species differences, ambient temperature, altitude, respiratory rate, and pulse-dose setting on the oxygen concentrator are factors that may have influenced the efficacy of the evaluated method. In the brown bears, pulsed delivery of oxygen from the concentrator increased PaO<sub>2</sub> as efficiently as low flows of continuous oxygen supplemented from oxygen cylinders, as previously described.<sup>14</sup> Advantages of the portable oxygen concentrator included small size and low weight, rechargeability, and ease of operation. Maintenance is simple, as it only requires cleaning of the air inlet filter. The evaluated concentrator cost approximately \$2,500 U.S. dollars in 2011, including a 3-yr warranty. Once purchased, electricity for recharging of the battery is the sole expense associated with running this device. In addition, it is a safer alternative than oxygen cylinders when using helicopters for wildlife capture, as the oxygen concentrator is a nonexplosive device. However, when high flow rates are required, or in conditions where oxygen concentrators do not function adequately, backup oxygen cylinders are needed.

Portable oxygen concentrators have oxygen-conserving devices with demand valves that provide oxygen during inhalation only.<sup>19,24</sup> They do not produce 100% oxygen, but the pulse-dose technology increases the efficiency of the device and prevents oxygen from being wasted. Oxygen delivered during the first part of the inspiratory effort has the most direct effect on gas exchange in the lungs. In comparison, during continuous-flow oxygen delivery, oxygen delivered during exhalation is wasteful. The setting on an oxygen concentrator with pulse-dose delivery is reflective of the bolus size (volume) in ml/breath, not a flow in L/min. In the manufacturer's product brochure for the EverGo concentrator, the settings are described as "pulse dose settings." Setting 1 delivers a 12-ml pulse volume, whereas setting 6 delivers a 70-ml pulse volume, and the maximum output is 1,050 ml/min for all settings. In contrast, in the EverGo User Manual, the same settings are described as "flow settings," which results in confusion to the operator. The settings on oxygen-conserving devices are often reported to be equivalent to a continuous flow.<sup>4,19</sup> However, this is a common misconception, as setting 2 does not mean "2 L/min." The pulse volume that corresponds to a setting and the maximum oxygen production per minute vary with different devices.<sup>4,9,24</sup> Other factors that affect equivalency in-

clude respiratory rate, tidal volume, and dead space.<sup>17</sup>

The pulse-dose setting on the EverGo concentrator should be adjusted according to the respiratory rate of the animal to deliver the maximum pulse volume of oxygen per breath. For example, setting 6 with a pulse volume of 70 ml can be used for a respiratory rate up to 15 breaths per minute, whereas setting 1 with a pulse volume of 12 ml can be used for a maximum respiratory rate of 88 breaths/min. However, a description of this is lacking in the manufacturer's user manual. Thus, based on assumed equivalency, the highest setting was incorrectly chosen for larger animals, independent of their respiratory rate, during the first study year. In 2010, the setting was adjusted according to the animal's respiratory rate. The lower respiratory rates and the less severe hypoxemia recorded in brown bears, compared to in bighorn sheep and reindeer, probably contributed to the greater increase in PaO<sub>2</sub> for the bears. Bench testing of portable concentrators and other oxygen-conserving devices has only been performed at respiratory rates between 10 and 35 breaths/min, which does not account for the wide variability in breathing patterns that occur in a clinical setting.<sup>3,9,24</sup> Still, variability in device performance related to pulse volumes at various breath rates was shown in those studies. Further in-depth assessment of device settings in relation to a wide range of respiratory rate is required. In the present study, during anesthesia of tachypneic bighorn sheep the concentrator alarmed that the respiratory rate was exceeding the capacity of the device, and it did not deliver pulse doses for each breath. During high respiratory rates, the efficiency of pulsed oxygen delivery may be negatively affected by relatively longer pulse delivery times and shallow breathing. If the total pulse delivery time is more than 70% of the inspiratory time, which may occur during high respiratory rates, oxygen is wasted in the anatomical dead space.<sup>9</sup> When breathing is shallow, trigger sensitivity of the device may be an important issue, as a certain pressure is needed for pulsed delivery of oxygen and the device may not be able to detect all inspiratory efforts.<sup>3</sup> In addition, the size and shape of the cannula nasal prongs can also affect trigger sensitivity.<sup>24</sup> Because smaller prongs do not occlude the nostrils as much as wider pronged cannulas, they may result in less resistance to air flow and thus a greater inspiratory flow may be needed to trigger oxygen delivery.

The high altitude and cold temperature that some bighorn sheep were anesthetized in were

near or below the recommended operating conditions of the concentrator. Thus, the oxygen concentration produced by the device may have been decreased. However, because it was not possible to measure the fraction of inspired oxygen (FiO<sub>2</sub>) in these conditions, the impact of temperature or altitude on delivered oxygen concentration could not be determined. In addition to the importance of knowing the limitation of devices used for oxygen therapy, it is also imperative to consider physiological factors that affect oxygenation. The limited increase in PaO<sub>2</sub> of the bighorn sheep during oxygen supplementation from the evaluated portable concentrator may only partly be due to limited capacity of the device to deliver oxygen to tachypneic animals. Shallow breathing increases dead space ventilation.<sup>23</sup> The efficacy of oxygen therapy is influenced by species-related physiological changes during anesthesia, such as the degree of intrapulmonary shunting, which is an extreme form of ventilation-perfusion mismatch. As shunt fraction increases, an elevation in FiO<sub>2</sub> becomes less effective at increasing the PaO<sub>2</sub>.<sup>2</sup> Both the bighorn sheep and the reindeer developed more severe hypoxemia than the brown bears. This is in agreement with previous studies showing that wild ungulate species become more hypoxemic than carnivores during anesthesia.<sup>5,14,21</sup> Domestic sheep sedated with medetomidine or other  $\alpha$ -2 agonists, or anesthetized with medetomidine-ketamine also experience severe hypoxemia and tachypnea.<sup>6,8</sup> Intrapulmonary shunting results in increased venous admixture and appears to be a common cause for  $\alpha$ -2 agonist-induced hypoxemia in domestic sheep, with a larger shunt fraction in sheep in lateral compared to sternal recumbency because additional shunting develop during lateral positioning.<sup>7,8,18</sup> In the bighorn sheep, hypoxemia developed because of high altitude, hypoventilation (increased PaCO<sub>2</sub>), and intrapulmonary changes. The increased P(A-a)O<sub>2</sub> (>15 mmHg) indicates that intrapulmonary changes (i.e., ventilation-perfusion mismatch including shunt, or diffusion impairment) contributed to hypoxemia. In addition, the lack of response to supplemental inspired oxygen further supports the presence of intrapulmonary shunting, because oxygen therapy becomes inefficient at shunt fractions above 50%.<sup>2</sup>

Pulse oximetry did not reliably indicate hypoxemia or normoxemia, or failed to produce a reading, in brown bears anesthetized with medetomidine-zolazepam-tiletamine in this study, as previously reported as well.<sup>14</sup> In some hypoxemic



bears, the pulse-oximetry-derived  $SpO_2$  values were over 90%, whereas the calculated  $SaO_2$  values were lower. Thus, pulse oximetry overestimated saturation at lower ranges, with the risk of undiagnosed hypoxemia if used as the sole monitor of oxygenation. During oxygen supplementation the  $SpO_2$  values were commonly lower than the  $SaO_2$  values, i.e., pulse oximetry was underestimating saturation and did not accurately reflect the effect of oxygen therapy. Analysis of arterial blood gases is considered the gold standard for measurement of arterial oxygenation, although it does not provide continuous data. The present study could have been strengthened by analysis of serial blood gas samples during oxygen supplementation, to show how quickly oxygen supplementation corrected hypoxemia and if it was adequately sustained. However, serial arterial sampling was not feasible due to other ongoing procedures and time restraints during handling of anesthetized animals in the field.

Although there was a statistically significant but small increase over time in the *mean*  $PaCO_2$  values of brown bears and bighorn sheep, there were individuals of both species that experienced a decrease in  $PaCO_2$  during oxygen supplementation. The study was not designed to look at the temporal effect of the anesthetic protocol; there were no control animals that did not receive oxygen supplementation. Therefore, it is difficult to determine if the increase in  $PaCO_2$  that some animals experienced was a temporal effect of the anesthetics or an effect of the oxygen therapy. In a study on physiologic evaluation in anesthetized brown bears that did *not* receive oxygen supplementation, an increase in  $PaCO_2$  over time was noted.<sup>13</sup> On the contrary, an increase in  $PaCO_2$  has been associated with oxygen therapy at 10 L/min in North American elk (*Cervus canadensis manitobensis*) anesthetized with xylazine-carfentanil.<sup>20</sup> The magnitude of increase in  $PaCO_2$  in the elk was much greater than in the current study. The exact mechanism for hypercapnia during oxygen therapy is not known and a topic of debate.<sup>1</sup> However, mild to moderate hypercapnia may be beneficial because it supports cardiovascular function, stimulates the sympathetic nervous system, and enhances the release of oxygen from hemoglobin into the tissues, whereas severe hypercapnia can lead to tachyarrhythmia, hemodynamic instability, and coma.<sup>10</sup>

## CONCLUSIONS

The evaluated portable oxygen concentrator with pulsed delivery effectively treated hypox-

emia in anesthetized brown bears and reindeer, whereas no or minor improvement in arterial oxygenation was recorded in bighorn sheep. The efficacy of oxygen therapy was influenced by limitations of the device and probably also by physiological changes in pulmonary function of the anesthetized animals. Portable oxygen concentrators have great potential for prevention and treatment of hypoxemia during anesthesia of animals in the field.

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