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SHORT COMMUNICATIONS

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Observations on the Use of Gonacon™ in Captive Female elk (*Cervus Elaphus*)

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ABSTRACT: Overabundant populations of elk (*Cervus elaphus*) are a significant concern in some areas of the western United States because of potential ecologic damage and spread of brucellosis to domestic livestock. *Brucella abortus* is transmitted among elk through direct contact with aborted fetuses, placentas and associated fluids, or postpartum discharge of infected animals. Because transmission of brucellosis is dependent on pregnancy, contraception of cows could be used for both disease and population management. The objective of this study was to evaluate the contraceptive efficacy of a gonadotropin-releasing hormone vaccine (GonaCon™) in female elk. In September 2004, cows were given a single immunization of either 1,000 μg ($n=12$) or 2,000 μg ($n=10$) of GonaCon™ and compared with a group of adjuvant-treated controls ($n=15$). In November 2004, 2005, and 2006, cows were grouped with bulls for the breeding season. Blood samples were taken in February 2005 and March 2006 and 2007 for pregnancy testing, progesterone assays, and antibody titers. For cows given 1,000 μg GonaCon™ the percentages that were infertile for 2005, 2006, and 2007 were 86%, 90%, and 100%, respectively, compared with 90%, 100%, and 100% for cows given 2,000 μg GonaCon™. Rates of infertility for control cows were 23%, 28%, and 0% ($P<0.0001$). The results indicated that either dose of GonaCon™ prevented pregnancy of elk cows for at least 3 yr. We concluded that GonaCon™ use for population management of elk warrants consideration as part of a strategy to control brucellosis.

Key words: Elk, *Cervus elaphus*, GnRH vaccine, GonaCon™, immunocontraception.

INTRODUCTION

In previous studies, we have demonstrated that the gonadotropin-releasing hormone (GnRH) vaccine, GonaCon™, is highly effective for preventing pregnancy in white-tailed deer (*Odocoileus virginianus*; Miller et al., 2000, 2007), feral horses (*Equus caballus*; Killian et al., 2004, 2006a), domestic and feral swine (*Sus scrofa*; Miller et al., 2003; Killian et al., 2006c), bison (*Bison bison*; Miller and Drew, 2004), as well as several other species (Levy et al., 2004; Miller and Killian, 2004; Nash et al., 2004). In female deer and horses, a single intramuscular injection of GonaCon™ was effective for up to 5 yr (Killian et al., 2006b; Miller et al. 2007). GonaCon™ stimulates the immune system to produce antibodies against GnRH, a small peptide protein produced by the hypothalamus. When sufficient antibody is present, the antibody complexes with, and inactivates, GnRH and prevents it from stimulating reproductive hormone and gamete production. The result is an infertile animal that remains in this state until the concentration of antibody declines to an ineffective level. In safety and toxicity studies with white-tailed deer, GonaCon™ had no adverse effects based on blood chemistry, postmortem, and histopathology evaluations (Killian et al., 2006a).

Contraceptive vaccines can be used as a tool to manage overabundant wildlife populations where lethal means of management are not feasible (Fagerstone et al., 2002), such as in national parks or urban or suburban areas. The contraceptive management strategy works best when populations have been reduced to the desired level before the use of contraceptive vaccines.

Overabundant wildlife populations also

increase the potential for disease transmission. Brucellosis is a zoonotic disease transmitted among elk, bison, and domestic livestock by direct contact with aborted fetuses, placentas, and associated fluids of infected animals. The disease is present in free-ranging elk and bison in the Greater Yellowstone Area (GYA; Cheville et al., 1998). Because the ranges of elk and bison may overlap with grazing cattle, there is considerable concern the disease will be spread to livestock. Although elk cows, under natural conditions, typically seek isolation during calving, winter feeding of elk and livestock has increased congregation and commingling, resulting in increased opportunities for disease transmission.

Miller and Drew (2004) and Killian et al. (2006c) introduced the concept that brucellosis transmission could be limited by preventing pregnancy in conjunction with a *Brucella* vaccination campaign in bison and feral swine. Reversible contraception could prevent pregnancy, and thus abortion, of *Brucella*-infected elk until they cleared the bacteria. We undertook the present study to evaluate the contraceptive efficacy of two doses of GonaCon™, given as a single injection to captive female elk.

The study was conducted at the Sybille Wildlife Research Unit of the Wyoming Game and Fish Department (Wheatland, Wyoming, USA; 41°45′47″N, 105°22′36″W) from 2004–2007. In February 2002, female elk calves were captured in corral traps at the National Elk Refuge (Jackson, Wyoming, USA) and transported to Sybille. There elk were housed in 0.4-ha corrals and fed alfalfa hay supplemented with a pelleted ration. Water and a trace mineral block were provided ad libitum. Chronic wasting disease has existed in the Sybille facility for more than 15 yr and captive cervids often contract the disease, probably from a contaminated environment (Miller et al., 2004) Chronic wasting disease has not been found where the calves were captured (Kreeger, unpubl. data).

The GonaCon™ vaccine consisted of GnRH peptide conjugated to Keyhole Limpet Hemocyanin (KLH; Miller et al., 2000) made into an emulsion with Adju-Vac™ adjuvant (Pocatello Supply Depot, Pocatello, Idaho, USA). In September 2004, 12 cows received a 1-ml injection of 1,000 μg of GonaCon™, 10 cows received a 1-ml injection of 2,000 μg of GonaCon™, 13 control cows received a 1-ml injection of the adjuvant-buffer emulsion, and two control cows were untreated. Treatment groups were housed in individual pens. Intramuscular injections were delivered remotely by darts equipped with biodegradable barbs (Pneu-Dart, Inc., Williamsport, Pennsylvania, USA).

At the beginning of November 2004, 2005, and 2006, cows were grouped with bulls for breeding. Bulls were exchanged among the cow groups every other week for 3 mo to maximize conception. Blood samples were collected in February or March of 2005, 2006, and 2007 from the jugular vein while cows were restrained in a chute. After clotting, the serum was harvested by centrifugation and kept stored frozen at −20 C until assay. Serum was used to determine antibody titers to GnRH and progesterone concentration using methods described elsewhere (Miller et al., 2000). Assays for pregnancy-specific protein B were performed by BioTracking (Moscow, Idaho, USA).

Significant differences among treatments and controls for percentages of infertility and mortality were determined by chi-square. Differences between treatments for antibody titers and serum progesterone concentrations were determined by Student's *t*-test.

Antibody titers for cows treated with 1,000 μg of GonaCon™ averaged 1.04×10^5 at 5 mo after the immunization. Average titers were maintained for the 1,000 μg group at 7.8 and 8.5×10^4 in 2006 and 2007, respectively (Fig. 1). Cows receiving the 2,000-μg dose of GonaCon™ had an average titer of 1.29×10^5 in 2005, which compared with average titers of 1.48 and 1.44×10^5 ($P=0.016$) in

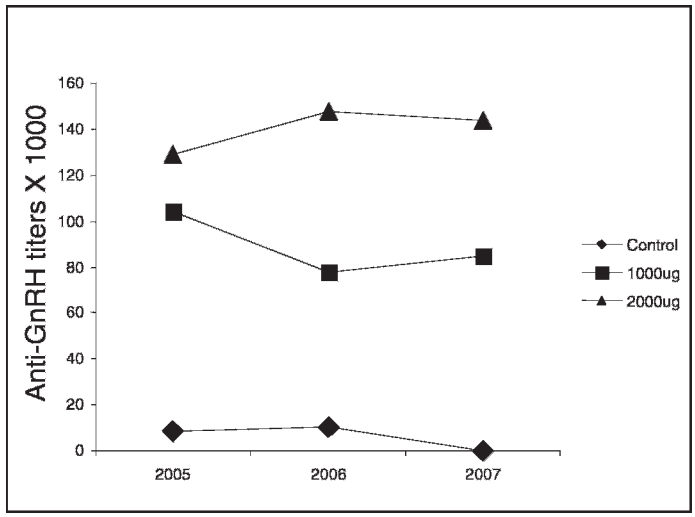

FIGURE 1. Average anti-GnRH titers for serum samples taken from control elk cows and from 1,000-μg, and 2,000-μg treated elk cows in February or March of 2005, 2006, and 2007, following a single vaccination with GonaCon™ or a control vehicle in September of 2004.

2006 and 2007 (Fig 1). These data suggested that there may be an advantage to using the 2,000-μg dose of GonaCon™ over the 1,000-μg dose to provide significantly greater titers.

Compared with the control animals, both doses of the GonaCon™ vaccine were highly effective in preventing pregnancy in elk cows throughout the entire study ($P<0.0001$). Annual infertility rates were lowest in the control animals where 27% (4/15), 25% (2/8), and 0% (0/6) were infertile in 2005, 2006, and 2007, respectively (Fig. 2). In contrast, 92% (11/12), 90% (9/10), and 100% (8/8) were infertile in the group receiving 1,000 μg of Gona-

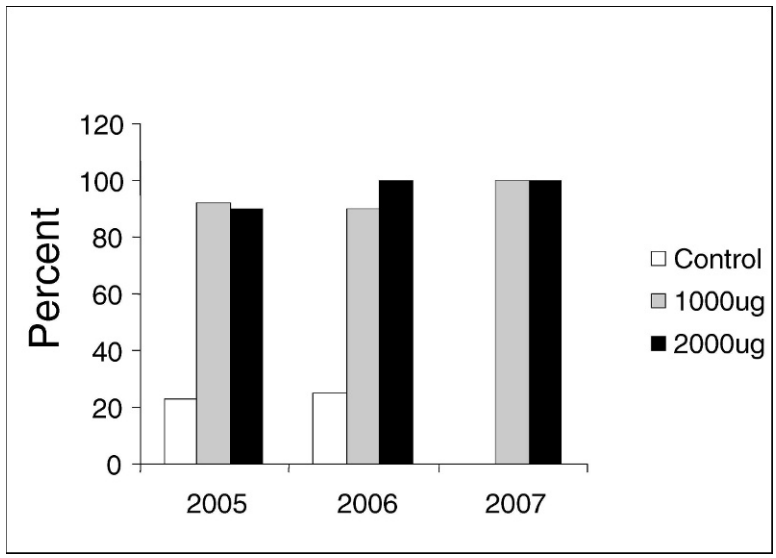

FIGURE 2. Average rates of infertility for control elk cows and for 1,000-μg and 2,000-μg treated elk cows for breeding seasons in 2005, 2006, and 2007, following a single vaccination with GonaCon™ in September of 2004.

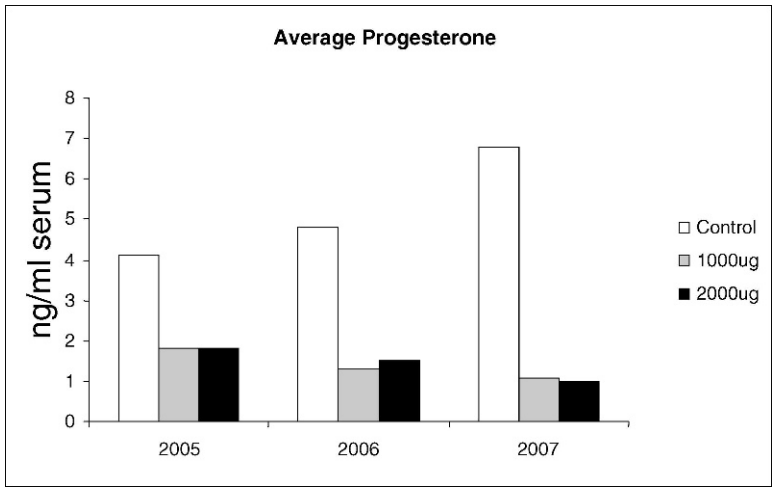

FIGURE 3. Average serum progesterone concentrations for control elk cows and for 1,000-μg and 2,000-μg treated elk cows for breeding seasons in 2005, 2006, and 2007, following a single vaccination with GonaCon™ in September of 2004.

Con™, and 90% (9/10), 100% (8/8), and 100% (6/6) were infertile in the group receiving the 2,000-μg dose of GonaCon™ (Fig. 2).

Although antibody titers were greater in cows treated with the 2,000-μg dose of GonaCon™, there were no differences in rates of infertility between the 1,000 μg and 2,000 μg GonaCon™ groups ($P = 0.697$) over the three breeding seasons studied. This outcome could change in future years if there is a greater decline in titers for the 1,000 μg group compared with the 2,000 μg group. Taken together, these results suggested that a single injection of either dose of GonaCon™ could be used for elk herds where population management by nonlethal means is desired.

Although some progesterone is secreted during the luteal phase of the estrous cycle, maximal serum concentrations of progesterone are produced by the corpus luteum during pregnancy. Control animals, most of which were pregnant when the blood samples were taken in February or March, had greater average concentrations of serum progesterone ($P<0.0001$) than cows treated with GonaCon™ (Fig. 3).

Because GonaCon™ was a highly effective immunocontraceptive vaccine for three breeding seasons, we suggest that it may prove useful in controlling brucellosis in infected elk herds' winter feed grounds in the GYA-concentrated elk, where the likelihood of disease transmission is increased. This is supported by the increased prevalence of *Brucella* antibodies in feedground elk, which is an order of magnitude higher than rates in elk not wintering on feed grounds (Kreeger, 2002). However, elk concentrated on feed grounds lend themselves to a large-scale vaccination program (Kreeger and Olsen, 2002). A challenge in managing elk in the GYA is that most herd sizes are higher than desired management levels, and hunting has been unable to reduce elk numbers. Thus, a single-dose, highly effective immunocontraceptive, like GonaCon™, would serve to reduce herd numbers while simultaneously preventing pregnancy and thus abortion, which would decrease transmission of brucellosis.

An unfortunate aspect of this study is that a large number of cows died. Of the cows that began the study in the fall of 2004, only 20 of the animals were alive when blood samples were taken in April of 2007. The cause of death in every instance

was CWD, diagnosed by immunohistochemistry. Exposure to the CWD prion was most likely environmental (Miller et al., 2004) because the facility has experienced continuous losses to CWD for more than 20 yr (Kreeger, unpubl. data).

Results of this study indicated that either dose of GonaCon™ prevented pregnancy of elk cows for at least 3 yr. We concluded that GonaCon™ use for population management of elk warrants consideration as part of a strategy to control brucellosis.

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