

Gonadotropin-releasing hormone vaccine (GonaCon-Equine) suppresses fertility in free-ranging horses (*Equus caballus*): Limitations and side effects of treatment

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In many areas of the western United States, overabundant and rapidly expanding feral horse (*Equus caballus*) populations pose a significant challenge for natural resource managers. There is wide-spread concern that unregulated feral horse populations are severely altering or degrading native plant communities. Controlling the fertility of female horses offers a potential strategy for limiting the growth of overabundant populations.

We evaluated the long-term effectiveness of GonaCon-Equine vaccine both as primary immunization and subsequent reimmunization four years later to suppress fertility in free-ranging female horses at Theodore Roosevelt National Park, North Dakota. In the fall of 2009, horses were gathered via helicopter and 57 adult mares were randomly assigned to either a treatment (n = 29; 2.0 mg GnRH conjugate + 2.0 mL adjuvant) or control (n = 28; 2.0 ml 0.9% saline) group. Females in both groups received an intramuscular injection in the gluteal musculature by hand-injection. Four years later, in 2013, horses were similarly gathered and revaccinated with the same doses. We determined the effectiveness, duration, and reversibility of vaccination with GonaCon on reproduction by comparing foaling rates of treated and control mares during 1 March to 31 December, 2009-2016. In conjunction with foaling observations, we also evaluated potential side effects of GonaCon on pregnancy, neonatal health and survival, injection site reactions, daily activity patterns and socio-sexual behaviors.

Foaling proportions in GonaCon-vaccinated mares, following the primary vaccination were lower than for control mares for the second (2011) (44.8% (13/29) vs 70.3% (19/27) (P = 0.047) and third (2012) (53.6% (15/28) vs 77.8% (21/27) (P = 0.053) post-treatment foaling seasons but were absent the fourth (2013) (73.1% (19/26) vs 69.2% (18/26) (P = 0.50) post-treatment season, demonstrating reversibility of the vaccine. However, the effectiveness of a single immunization, measured as the percent decrease in foaling when compared with control mares, was low to modest; estimated at 36.3% and 31.1%, in years 2 and 3, respectively. In contrast, revaccination with GonaCon, four years post-primary treatment was 100% (0/25) effective in suppressing fertility, whereas mean foaling rate of control mares was 84% (21/25) (95% CI = 65.3-93.6%) in 2015 and 2016. The effectiveness of revaccination persisted, although slightly diminished, during the second year (2016) at 80.9% (16% (4/25) foaling rate; 95% CI = 6.4-34.6).

With the exception of non-debilitating inflammation at the vaccine injection site, no other adverse effects were observed. These data indicate that GonaCon-Equine can be effective in suppressing fertility in free-ranging horses when both a primary immunization and booster are administered. Ongoing research will inform the optimum revaccination schedule for effective contraception.