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Concomitant administration of GonaCon™ and rabies vaccine in female dogs (Canis familiaris) in Mexico☆

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ABSTRACT

Mexico serves as a global model for advances in rabies prevention and control in dogs. The Mexican Ministry of Health (MMH) annual application of approximately 16 million doses of parenteral rabies vaccine has resulted in significant reductions in canine rabies during the past 20 years. One collateral parameter of rabies programs is dog population management. Enhanced public awareness is critical to reinforce responsible pet ownership. Surgical spaying and neutering remain important to prevent reproduction, but are impractical for achieving dog population management goals. GonaCon™, an anti-gonadotropin releasing hormone (GnRH) vaccine, was initially tested in captive female dogs on the Navajo Nation, 2008. The MMH led this international collaborative study on an improved formulation of GonaCon™ in captive dogs with local representatives in Hidalgo, Mexico in 2011. This study contained 20 bitches assigned to Group A (6 control), Group B (7 GonaCon™), and Group C (7 GonaCon™ and rabies vaccine). Vaccines were delivered IM. Animals were placed under observation and evaluated during the 61-day trial. Clinically, all dogs behaved normally. No limping or prostration was observed, in spite of minor muscle atrophy post-mortem in the left hind leg of dogs that received GonaCon™. Two dogs that began the study pregnant give birth to healthy pups. Dogs that received a GonaCon™ injection had macro and microscopic lesions consistent with prior findings, but the adverse injection effects were less frequent and lower in intensity. Both vaccines were immunogenic based on significant increases in rabies virus neutralizing antibodies and anti-GnRH antibodies in treatment Groups B and C. Simultaneous administration of GonaCon™ and rabies vaccine in Group C did not affect immunogenicity. Progesterone was suppressed significantly in comparison to controls. Future studies that monitor fertility through multiple breeding cycles represent a research need to determine the value of integrating this vaccine into dog rabies management.

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1. Introduction

Mexico is a global model for advances in rabies prevention and control in dogs (Canis familiaris). During the past 20 years the Mexican Ministry of Health (MMH) has applied approximately 16 million doses of parenteral canine rabies vaccine annually, resulting in a substantial reduction in canine rabies [1,2]. This accomplishment not only illustrates the effectiveness of these campaigns, but also brings the elimination of canine rabies into focus as a potentially achievable goal in developing countries. However, effective dog population management is central to achieving that goal. Clearly, enhanced public awareness is critical to reinforce the key role of responsible pet ownership to reduce the risks associated with dog overpopulation to human and animal health. Spaying and neutering remain important components to prevent unwanted reproduction, but they are expensive, invasive, time consuming and impractical for achieving broader dog population management goals integral to canine rabies elimination [1,3]. Fertility control holds promise as an efficient and less invasive method in rabies management in Mexico and perhaps globally.

México maintains a close relationship with the U. S. Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS) through the North American Rabies Management Plan, signed by representatives of Canada, Mexico, the Navajo Nation and the U.S. in 2008. This plan serves as a basis for collaborations to develop, study and implement methods and strategies to enhance rabies management. The immunocontraceptive vaccine GonaCon™ represented an ideal candidate for evaluation in captive dogs in Mexico [4,5]. Results from this study should provide a foundation for continued evaluation of GonaCon™ as a prospective method for dog population management.

The MMH and USDA, APHIS, Wildlife Services (WS), with technical support of many partners, collaborated in a study of a new formulation of GonaCon™ in captive dogs in Mexico. The study was conducted in Hidalgo State in collaboration with State Health Services, and invited institutions and groups. The primary objectives were to: (1) determine the immunogenicity of simultaneous IM administration of GonaCon™ and rabies vaccine and (2) assess potential adverse health effects in dogs, including injection site reactions from this new vaccine formulation.

2. Materials and methods

2.1. GonaCon™ and canine rabies vaccine

GonaCon™ is an immunocontraceptive vaccine (USDA, APHIS, Wildlife Services (WS), National Wildlife Research Center (NWRC), Fort Collins, CO, USA) consisting of mammalian gonadotropin releasing hormone (GnRH) conjugated to a large mollusk hemocyanin protein and emulsified with the adjuvant AdjuVac™. Unlike prior GonaCon™ formulations, the one used in this study was produced in a clean room to reduce the chance of particulate contamination and Gentamicin and Fungizone (Life Technologies, Carlsbad, CA) were added to inhibit bacterial and fungal activity. Each 0.5 ml dose contained 500 μg of the GnRH conjugate and 21 μg of inactivated Mycobacterium avium in the adjuvant. GonaCon™ was stored and shipped under refrigerated conditions in pre-loaded, 3 ml Air-Tite luer-lock syringes (Air-Tite Products, Virginia Beach, VA, USA) [5].

A commercial inactivated rabies virus vaccine was administered (Rabiffa, Merial Inc., El Marques, Qro., Mexico) that is commonly used by the State Health Services during the National Weeks of Dog Rabies Vaccination in accordance with Mexican Regulations. By special request from the MMH, the rabies vaccine was supplied in 20 ml vials containing 20 dosages (1 ml/dose), stored at 4 °C until ready for use [6].

Fig. 1. Stray dogs housed and cared for at PROVEZA's Shelter and Refuge (Cerrada 16 de Septiembre s/n Colonia Centro, Villa de Tezontepec, C.P. 43882, Hidalgo, Mexico) included in Group B of the GonaCon™ study in Mexico 2011.
Photo taken by Dr. Luis Lecuona.

2.2. Vaccine administration

Vaccines were administered once IM throughout this study in the upper right hind leg (rabies vaccine) or upper left hind leg (GonaCon™). A 3 ml disposable syringe and 21 G × 38 mm needle were used to administer vaccines.

2.3. Experimental animals

Twenty female dogs of mixed breeds were collected from September to November 2010 for this trial. Six owned bitches came from the Villa de Tezontepec County, in Hidalgo State. The 6 owners signed an authorization for inclusion of their dogs in the study. Fourteen other bitches were collected at dog round-ups conducted by the Canine Attention Centers from the Sanitary Regions of Pachuca and Tulancingo in Hidalgo State. Typically, unclaimed dogs at the Canine Attention Centers are euthanized in a 48–72 h post round-up pursuant to the National Animal Control Regulation (NOM-042-SSA2-2006. Number 4.2.14, Section 4.2.) [7]. Fourteen bitches over 1 year old were selected from this source for this study. Dogs were selected based size (medium or large), apparent healthy clinical status and general body condition. Dogs were held for a 60-day observation and adaptation period.

Six bitches in Group A were confined at the home of their owner. The other 14 bitches were divided into vaccination Group B (GonaCon™) or Group C (GonaCon™ and rabies). These groups included 7 animals maintained in communal kennels in the PROVEZA's Shelter and Refuge (Cerrada 16 de Septiembre s/n Colonia Centro, Villa de Tezontepec, C.P. 43882, Hidalgo, Mexico; 19° 52′ 45.33 N, 98° 49′ 13.36″ W) (Fig. 1). This facility offered complete dog holding support during this study. Each bitch was marked with a collar and unique numbered tag for identification. Animal care personnel maintained the kennels twice/day. Dogs were fed a commercial dog food (Adult Natural Balance Pedigree, Mars Inc., Mexico) and water ad libitum. All female dogs were evaluated by veterinarians, State Health Services, Hidalgo during the 61-day study.

The 6 owned bitches chosen for Group A were vaccinated with the rabies vaccine. The 14 female dogs maintained in the PROVEZA's Shelter and Refuge were randomly assigned to two treatment groups. Group B included 7 dogs that were vaccinated