Comparison of intratesticular injection of zinc gluconate versus surgical castration to sterilize male dogs

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Objective—To compare castration of dogs by use of intratesticular injection of zinc gluconate with traditional surgical procedures in terms of acceptance by pet owners, ease of use, and short-term outcomes on Isabela Island of the Galápagos Islands.

Animals—161 privately owned male dogs admitted to a neuter program.

Procedures—Medical records of male dogs neutered during a 4-week animal control campaign were reviewed to collect information regarding signalment, method of castration, complication rate, and treatment outcomes.

Results—Of the 161 dogs admitted for castration, 58 were surgically castrated and 103 were treated with zinc gluconate. Dogs were returned to their owners for observation following castration. Wound dehiscence occurred in 2 skin incisions, representing 3.4% of the 58 dogs that underwent bilateral orchiectomy. Necrotizing zinc-gluconate injection-site reactions occurred in 4 dogs receiving injection volumes near the maximum label dose (0.8 to 1.0 mL), representing 3.9% of the zinc-gluconate procedures. Surgical wound complications were treated by superficial wound debridement and resuturing, in contrast to zinc-gluconate injection-site reactions, which all required orchiectomy and extensive surgical debridement, including scrotal ablation in 2 dogs.

Conclusions and Clinical Relevance—Low cost, ease of use, and cultural acceptance of a castration technique that does not require removal of the testes make zinc gluconate a valuable option for large-scale use in dogs, particularly in remote locations lacking sophisticated clinical facilities or skilled surgeons and staff. Further investigation is needed to identify risk factors in dogs for adverse reactions to zinc gluconate and to develop strategies for avoidance. (*Am J Vet Res* 2008;69:140–143)

Isabela Island is the largest island of the Galápagos archipelago and has the greatest diversity of endemic animal species. The island is best known for its population of endangered giant tortoises, marine iguanas, and Darwin finches. Most of the 1,500 residents of Isabela Island inhabit the fishing village of Puerto Villamil, and a smaller number live on farms in the highlands. Although not native to the Galápagos Islands, many dogs and cats are kept as pets and are allowed to roam freely.[1,2] Most dogs and many cats are friendly and are perceived as pets owned by individual families but generally do not reside indoors. Cats are also present as free-roaming neighborhood strays or are clearly feral.

Nonnative introduced species are a constant threat to the unique biodiversity of the archipelago.[3] A major concern on Isabela Island is predation of endangered marine iguanas by free-roaming dogs and of birds by cats.[1,2] Poisoning and hunting campaigns have been used to eradicate invasive domestic species, including goats, pigs, donkeys, cattle, poultry, cats, and dogs on various Galápagos islands.[3,4] A brief trial of nonsurgical castration of male dogs with intraepididymal injection of chlorhexidine digluconate was tested on Floreana Island 2 decades ago but was not adopted as policy.[5,a]

In 2004, a novel partnership to control the dog and cat population in the Galápagos Islands by neutering was initiated between the animal welfare group Animal Balance,[b] the Galápagos National Park Service, the Galápagos Quarantine and Inspection System, and the municipal Control and Management of Introduced Species Committee. The first spay-neuter program was conducted on Isabela Island during May 2004. In addition to neutering, an educational program was developed to promote responsible pet ownership and to encourage residents to restrict their dogs from roaming in environmentally sensitive areas.

Zinc gluconate[c] is a nonsurgical alternative to bilateral orchiectomy for castration of male dogs. This zinc compound, which is neutralized by arginine, is delivered by intratesticular injection, which results in sclerosis of the testes and permanent sterility. The product first became available for use in the United States in 2003, but by 2005 it was no longer in production, and the patent holder and the distributor severed their ties.[d] The product is still licensed for use by the FDA and is expected to reemerge when a new marketing partner-

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ship is arranged. Zinc gluconate is currently approved only for use in puppies 3 to 10 months of age with testes measuring 10 to 27 mm in width, but it has been used off-label in younger puppies and large adult dogs as well.

The advantages of nonsurgical castration of dogs in remote locations like the Galápagos Islands include less technical administration compared with surgery, lack of a requirement for anesthesia or surgery packs, and avoiding removal of the testes, which is widely viewed as unacceptable in some cultures. The purpose of the study reported here was to describe the use of nonsurgical castration with zinc gluconate and to compare it with traditional surgical castration in terms of acceptance by dog owners, ease of use, and short-term outcomes.

Materials and Methods

Data collection—Medical records of male dogs neutered during the May 2004 animal control campaign were reviewed. Information regarding signalment, method of neutering, complication rate, and treatment outcomes was retrieved from the medical records.

Sterilization project—Dogs were presented for castration by their owners. In addition to castration, each dog was treated with selemectin[e] for control of internal and ectoparasites. All dogs were implanted with a subcutaneous microchip and photographed for individual identification.[f] As a secondary objective, the project included education on responsible ownership and confinement of dogs to reduce their negative impact on the native flora; dogs were provided with collars and leashes and obedience training classes were offered. Equipment and supplies for the project were brought to the island by ship,[g] and a temporary neuter clinic was established in the village of Puerto Villamil in a building provided by the Galápagos National Park Service. The clinic had electricity and running water. Within the clinic facility, it was possible to provide injectable and isoflurane anesthesia and to perform sterile surgery. In addition to bilateral orchiectomy, zinc gluconate was included as a nonsurgical alternative. Supplies and personnel were also transported by truck to farms in the highlands of the island, where zinc gluconate was administered to dogs on-site. Program representatives remained on Isabela Island for 1 week following the last surgery to provide follow-up care as needed.

Anesthesia—Anesthesia for dogs undergoing surgery was induced by IV administration of ketamine and diazepam and maintained with isoflurane administered via endotracheal intubation. All dogs undergoing surgery were provided postoperative analgesia with carprofen[h] (4 mg/kg, SC, once). Dogs treated with zinc gluconate were not anesthetized, but dogs that appeared apprehensive were sedated with medetomidine[i] (40 µg/kg, IM).

Surgery—Dogs were prepared for surgery by clipping the hair from the inguinal area and cleansing the skin with povidone-iodine scrub solution and isopropyl alcohol. A spray of povidone-iodine solution without soap was applied as a final step. The surgical site was draped, and surgeons wore caps, masks, and sterile gloves, but not gowns. A separate autoclaved instrument pack was used for each patient. Absorbable suture material was used during standard techniques for bilateral orchiectomy. The incision was closed by placement of absorbable sutures intradermally to avoid the need for cutaneous suture removal at a later time.

Zinc-gluconate treatment—Zinc gluconate was provided as a sterile aqueous solution containing 0.2M zinc gluconate (13.1 mg/mL) neutralized to pH 7.0 with 0.2M L-arginine in glass vials containing 2 mL of ready-to-use solution.[c] The drug was supplied with plastic calipers and instructions for measuring the width of each testicle; a dosing chart was used to correlate testicular width (10 to 27 mm) with volume of zinc gluconate (0.2 to 1.0 mL).[6] In this project, dogs of all ages were treated by following the product label recommendation for volume of injection. Dogs with testes measuring < 10 mm in width received zinc gluconate volumes of 0.1 mL/testicle. Volumes for dogs with testes measuring > 27 mm in width were truncated at 1.0 to 1.1 mL/testicle (1.0 mL is the highest approved dose). Dogs were prepared by gently cleaning the scrotum with soap and water, but scrubbing and alcohol application were avoided. Two doses (tuberculin syringes with 5/8-inch 28-gauge needle) were prepared for each dog with the volume in each syringe calculated from each testicular width measurement. The needle was inserted into the dorsocranial aspect of each testicle and directed caudally so that the tip was estimated to be at the center of the testis, and the solution was gently injected. Two of the individuals administering the zinc gluconate had extensive previous experience, whereas 6 other individuals had not previously used the drug.

Follow-up—Dogs were released from the clinic to their owners at the end of the day. Dogs treated with zinc gluconate on the highland farms were released immediately after injection. No attempts were made to confine the dogs or to prevent licking and chewing of the incisions or injection sites.

Results

Medical records of 161 male dogs that were neutered during May 2004 were reviewed. Zinc gluconate was selected more frequently than bilateral orchiectomy by dog owners, who often cited desires to retain perceived protective and hunting behaviors and to avoid anesthesia as their reasons for selecting nonsurgical castration. Of the 161 dogs, 103 (64.0%) were treated with zinc gluconate and 58 (36.0%) were surgically castrated. Of 103 zinc-gluconate–treated dogs, 16 (15.5%) received small volumes (0.1 to 0.2 mL), 24 (23.3%) received intermediate volumes (0.3 to 0.7 mL), 52 (50.5%) received large volumes (0.8 to 1.1 mL), and 11 (10.7%) did not have a dose recorded. Most dogs were neutered in the temporary clinic in Puerto Villamil, but 20 dogs were treated with zinc gluconate at highland farms. Use of zinc gluconate was simple, quick, and well accepted by the dogs, which rarely had signs of injection pain.

Mild complications such as incisional or injection-site swelling were not consistently reported by owners. Moderate complications associated with bilateral orchiectomy were limited to wound dehiscence in 2 skin incisions, representing 3.4% (2/58) of dogs that underwent surgery. Necrotizing zinc-gluconate injection-site reactions occurred in 4 dogs, representing 3.9% (4/103) of dogs that underwent the zinc-gluconate procedure. All 4 dogs with severe zinc-gluconate reactions were large mature dogs that had received a dose of the drug at the upper end of the label range (3 dogs received 0.8 mL/testicle and 1 dog received 1.0 mL/testicle). Dogs with zinc-gluconate reactions were first examined at 4 to 6 days after treatment. The scrotum was swollen and contained a single draining tract in 2 dogs. Another dog had bruising and a draining tract in the prepuce several centimeters cranial to the testicular injection site. A fourth dog had chewed a portion of the scrotum and testicular tissue away.

Although the complication rate was similar for surgical and zinc-gluconate castration, the zinc-gluconate reactions were more severe. Surgical wound complications were treated by superficial wound debridement and resuturing. In contrast, zinc-gluconate reactions required antimicrobial treatment, orchiectomy, and extensive surgical debridement and reconstruction, including scrotal ablation in 2 dogs. These reactions occurred following administration by both experienced and novice individuals. All dogs made a full recovery following treatment of zinc-gluconate reactions and incisional dehiscences.

Discussion

The neuter program was well accepted by pet owners on Isabela Island. Of the island's total estimated dog and cat population, 67.4% were neutered during the first campaign in May 2004. A low rate of treatment complications was observed, and all of the dogs and cats made a full recovery from neutering procedures. The most severe complications were necrotizing tissue reactions that occurred in a small number of adult male dogs treated with zinc gluconate.

In prelicensing pilot studies using 4- to 6-month-old Beagles treated with zinc gluconate, swelling occurred 24 to 48 hours after treatment, and scrotal ulcers or testicular necrosis developed in 6.7% to 23.8% of dogs.[7] Mean testis, epididymis, and prostate gland weights were lower in treated dogs than in control dogs. Basal testosterone concentration initially decreased in most treated dogs but was similar to untreated control dogs at 24 months after treatment. In a subsequent field trial conducted with 270 puppies at humane societies and private veterinary practices, 2 dogs (0.7%) developed ulcers and 2 dogs that were initial treatment successes appeared to recover fertility by 12 months after treatment.[7] Collectively, efficacy (defined as no or low numbers of viable sperm in ejaculates) was 96.7% to 100% in licensing trials.[6,7]

Public health officials and veterinarians in Mexico collaborated on a large field trial to administer zinc gluconate to 10,000 adult pet dogs in 3 Mexican states.[j] In that trial, moderate discomfort was observed the first 1 to 2 days following treatment in some dogs. Interim analysis of adverse events prior to completion of the study revealed ulcer formation at the injection site in 2.6% of dogs.

Zinc gluconate has also been used in large-scale outpatient clinics in the United States.[k,l] More than 200 dogs have been treated at some of the single-day events. Organizers recommend implanting an identification microchip or tattooing an N in the ear to identify the neuter status of dogs given that these dogs still have testes after treatment. Most microchip identification systems currently used in the United States are able to register use of zinc gluconate in their databases, so the neuter status of dogs can be verified even if the owner cannot be located.[k] In some jurisdictions, veterinary practice acts or animal control regulations may need to be revised to recognize nonsurgical procedures as compliant with neuter regulations.[m]

The lack of complete testosterone suppression following treatment with zinc gluconate can be considered either a positive or a negative feature. One purpose of bilateral orchiectomy is to suppress undesirable aggressive and sexual behaviors and medical conditions associated with testosterone production, and zinc gluconate may not always achieve this goal. However, 2 reasons cited by many dog owners for opposing bilateral orchiectomy are anthropomorphic empathy regarding emasculation and a fear that desired behaviors such as protection and hunting instinct will be decreased by castration.[8,9] Preservation of testosterone production and presence of testes following castration may be viewed as desirable by these owners.

Proper injection technique is critical when zinc gluconate is used because leakage or injection into nontarget tissues can result in severe tissue damage. The needle should be changed following filling of the syringe and then inserted into the dorsocranial portion of the testicle beside the head of the epididymis. The indicated target for zinc-gluconate deposition is the center of the testicular tissue. Scrotal swelling and tenderness are common in the first few days following injection and usually resolve without treatment.[7] A more serious effect is the development of scrotal ulcers or draining tracts in the scrotal or preputial area. Self-trauma can be severe in these circumstances. Lesions are not necessarily restricted to the injection site, indicating that the solution may diffuse beyond the target area in some instances. In the study reported here, ulcers were restricted to 4 dogs receiving injection volumes near the maximum label dose (0.8 to 1.0 mL). However, because previous reports[j,l] have included ulcer formation in dogs receiving smaller doses it is not clear if injection volume influences risk of ulcer formation. Complications are possible regardless of whether nonsurgical or surgical castration is used, so neuter programs should have plans in place to provide follow-up and intervention should complications occur.

Possible contributing causes to complications in dogs treated with zinc gluconate in the Galápagos Islands include improper injection technique, improper after-treatment management, and characteristics unique to the Galápagos environment. In this project, dogs were returned to their free-roaming environment within hours of treatment. They were physically active

and were not restrained from irritating the injection site. A few dogs were observed to be breeding in the days following treatment. The warm climate and the habit of the dogs to lie on the hot sand and lava rocks may have contributed to vasodilation and tissue perfusion alterations that contributed to local toxic effects of the drug.

The low cost, ease of use, and cultural acceptance of a castration technique that does not require removal of the testes make zinc gluconate a valuable option for large-scale use, particularly in remote locations lacking sophisticated clinical facilities or skilled surgeons and staff. Further investigation is needed to identify risk factors for adverse reactions to zinc gluconate and to develop strategies for avoidance.

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