COMPARISON OF 4.7-MG DESLORELIN IMPLANTS AND SURGERY FOR THE TREATMENT OF ADRENOCORTICAL DISEASE IN FERRETS

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Abstract

Ferrets exhibiting overt clinical signs consistent with adrenocortical disease (ACD) were separated into 2 treatment groups. One group received surgical therapy (n = 28), whereas the other group was administered a 4.7-mg deslorelin acetate implant (n = 35). Each group was evaluated for clinical response to therapy and time to return of overt disease signs. The mortality rate was calculated for the deslorelin group and for a larger pool of surgical cases (n = 54). This larger surgical group included ferrets for which follow-up to evaluate time to return of disease was not possible. The time from treatment to return of ACD signs was longer for ferrets in the deslorelin group (16.5 months) compared with the surgery group (13.6 months). Three ferrets from the surgery group showed no response to the treatment provided. All ferrets in the medical group responded to deslorelin, although the shortest period of efficacy was only 3 months for 1 ferret. Of the ferrets in the surgery group, 3 (5.5%) died within 24 hours of the procedure. No ferrets died as a direct result of implantation with deslorelin. Although there may be distinct advantages of one modality over the other for any specific patient (e.g., surgery to investigate known or suspected concurrent disease), these results suggest deslorelin is an effective and safe treatment for ACD that should be considered when surgical intervention carries significant risk.

Key words: adrenocortical disease; deslorelin; ferret; implant; *Mustela putorius furo*

Adrenocortical disease (ACD) is a common disorder in the spayed/neutered pet ferret characterized by hyperplasia or neoplasia of the adrenal gland and overproduction of estradiol, 17-hydroxyprogesterone, and androstenedione. In some cases, tumors can become large or locally invasive or metastasize. Clinical signs associated with ACD in ferrets may include alopecia, pruritus, thinning skin, aggression, increased sexual behavior, prostate disease in males, vulvar enlargement in females, weight loss, and lethargy. The high incidence of ACD in the pet ferret has been linked to early-age spaying and neutering, which occurs at approximately 5 weeks of age in breeding farms in the United States. Delaying spaying and neutering has been found to simply delay the onset of ACD.[1] In theory, ACD is thought to develop due to chronic stimulation of the adrenal cortex by luteinizing hormone and follicle-stimulating hormone.[2]

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Treatment of ferrets diagnosed with ACD includes surgical removal or debulking of the affected adrenal gland(s), medical therapy for control of overproduction of the inciting hormones, or both in combination. Response to therapy is often assumed by resolution of the overt clinical signs associated with the disease and is supported by a reduction in circulating hormone (estradiol, 17-hydroxyprogesterone, and androstenedione) levels.

Surgical treatment of adrenal disease is well described. It is considered moderately to significantly challenging, with difficulty depending on a number of factors, including overall patient condition, location of the affected gland, size and presence of local invasion into the vena cava or other surrounding tissues, and presence of metastases. Swiderski et al[3] reported 1- and 2-year survival rates for 130 cases of ferrets treated surgically for hyperadrenocorticism; the 1-year survival rate was 98%, and the 2-year survival rate was 88%. Survival rate did not appear to be dependent on histopathologic characteristics of the abnormal adrenal gland; whether the right, left, or both glands were affected; or surgical technique, including complete versus partial excision. An earlier study in 1999 examined recurrence rates in 56 ferrets after adrenalectomy described as "subtotal bilateral adrenalectomy, or unilateral adrenalectomy followed by contralateral unilateral subtotal adrenalectomy."[4] The recurrence rate was 15%, with an average long-term follow-up period of 30 months.

Numerous medical therapies for ferrets have been described, including leuprolide acetate (Lupron Depot; Abbott Laboratories, Abbot Park, IL USA), melatonin, and others.[5] Treatment with leuprolide acetate, a gonadotropin-releasing hormone agonist, was reported as early as 2001, and its use is widespread and promising.[6] Johnson-Delaney[5] reported that the 30-day depot caused sex steroid suppression in intact ferrets for 30 days. In ferrets with ACD, Wagner et al[7] reported significant reduction in sex hormone levels and resolution of clinical signs, with recurrence at an average of 3.7 months (minimum-maximum, 1.5-8 months) after injection. A 2006 study showed a resolution of clinical signs associated with ACD for at least 8 months after oral administration of melatonin.[8] Other drugs targeting sex hormones have been described for use in the ferret as well, including flutamide (Eulexin; Schering-Plough, Kenilworth, NJ USA), finasteride (Proscar; Merck and Co., Inc., Whitehouse Station, NJ USA), and bicalutamide (Casodex; AstraZeneca, Wilmington, DE USA). Anecdotal reports indicate variable efficacy of these compounds.[5] There is little evidence that any medical therapy has any significant effect on the developing adrenal tumor.

Deslorelin (Suprelorin; Peptch Animal Health, North Ryde, Australia) was introduced as a medical therapy for ACD in 2005.[9] Wagner et al[9] described the effects of a subcutaneous 3-mg implant in 15 ferrets with confirmed ACD. Both clinical signs and measured plasma hormone concentrations significantly decreased after implantation. The mean time to recurrence was 13.7 ± 3.5 months (minimum-maximum, 8.5-20.5 months). The 3-mg deslorelin implant did not prevent adrenal tumor growth, because one-third of the ferrets had adrenal tumors that continued to grow while receiving deslorelin treatment.[9] Similar results were found in 30 ferrets treated with subcutaneous 4.7-mg deslorelin acetate implants.[10] The mean time to recurrence of clinical signs was 17.6 ± 5 months (minimum-maximum, 8.0-30 months). These animals had variable changes in adrenal size during treatment, from a reduction in adrenal size in some ferrets to mild enlargement of adrenal glands in most ferrets. Large tumors developed before clinical relapse in 2 (6.7%) of 30 animals implanted with the 4.7-mg deslorelin acetate product.[10]

Currently, discussion exists on the respective advantages of surgical versus medical therapy for treatment of ACD in ferrets. Advantages cited for surgical therapy include the potential for complete cure, the identification of local tumor infiltration or metastasis, and the opportunity to identify and potentially correct concurrent abnormalities, including pancreatic masses, trichobezoars, hepatobiliary disease, and other neoplasms. Disadvantages are those related to any potentially challenging abdominal surgery in a compromised patient and include deterioration of clinical condition, especially in patients with concurrent disease, and death. The purpose of this pilot study was to determine whether there are differences in the outcomes (return to clinical signs and mortality rate) of surgical therapy versus deslorelin implant treatment in ferrets diagnosed with ACD.

METHODS

Medical records were examined from 2 separate veterinary facilities (Avian and Exotic Animal Clinic, Indianapolis, IN USA, and Division of Laboratory Animal Resources, University of Pittsburgh, Pittsburgh, PA USA). Time to recurrence