Long-term prospective evaluation of topically applied 0.1% tacrolimus ointment for treatment of perianal sinuses in dogs

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**Objective**—To evaluate effectiveness of a combination of topically applied tacrolimus, orally administered prednisone, and a novel-protein diet for treatment of perianal sinuses in dogs and to monitor clinical progress and owner management of the condition for 2 years.

**Design**—Noncontrolled clinical trial.

**Animals**—19 dogs with perianal sinuses.

**Procedures**—Perianal sinuses were diagnosed during physical examination, and dogs were placed on a 16-week treatment protocol consisting of topically applied 0.1% tacrolimus ointment, orally administered prednisone (tapering dose), and a novel-protein diet. Metronidazole was orally administered for the first 2 weeks. Anal sacculectomy was recommended whenever anal sacs were involved. Dogs were evaluated every month for the first 4 months and then every 6 to 12 weeks for 2 years.

**Results**—Perianal sinuses resolved completely in 15 of 19 dogs during the 16 weeks. In the remaining 4 dogs, the lesions markedly improved but failed to completely resolve. Three of these had anal sac involvement, and the owner of 1 dog had complied poorly with treatment instructions. During the 2 years following treatment, all dogs were maintained on intermittently applied tacrolimus ointment, 4 dogs also received prednisone every other day, and 11 dogs remained on the novel-protein diet. At the conclusion of the study, 13 of the 15 dogs that survived to that point were free of perianal disease.

**Conclusions and Clinical Relevance**—The described protocol was effective and economical for resolving perianal sinuses. Dogs maintained on intermittent medications were unlikely to redevelop lesions. When the anal sacs were involved, anal sacculectomy appeared to improve the outcome. (J Am Vet Med Assoc 2009;235:397–404)

The condition of perianal sinuses (also known as anal furunculosis, perianal fistulae, pararectal fistulae, anusitis, or fistulae-in-ano) is an insidiously progressive, chronic inflammatory disease of the perianal and perirectal tissues in dogs, most commonly German Shepherd Dogs. The disease is characterized by deep suppurative ulcers and abscesses of the perianal region. Clinical signs usually include tenesmus, dyschezia, licking of the perineum, bleeding from the anal area, and malodorous, mucopurulent discharge. Bowel movements are often loose or frequent, but constipation may also develop. Affected dogs may have no clinical signs, but generally this disease is debilitating for the affected dogs and distressing for their owners.

Several hypotheses have been tested regarding the etiology of the disease and the predisposition of German Shepherd Dogs, generally without yielding much insight. Studies have been conducted to assess tail conformation, anal anatomy, bacterial involvement, histologic changes in anal tissues, thyroid gland function, concurrent colitis, and various immune dysregulations in affected dogs. Whereas local environment may play a role in the perpetuation and exacerbation of perianal sinuses, identification of a specific primary cause remained elusive for many years. However, results of recent studies suggest that an inappropriate T-cell–mediated inflammatory response is involved and that the predisposition in German Shepherd Dogs reflects a probable genetic component.

As usual with a disease that is difficult to cure, various methods have been used to manage perianal sinuses. Local cleansing and topical and systemic antimicrobial treatment are palliative only, and historically, surgery was performed after this approach failed. Radical excision of the lesions (with and without anal sacculectomy), anal resection with rectal pull-through, deroofing and electrofulguration, chemical cauterization, cryotherapy, caudectomy, and laser excision are all surgical approaches to treatment. Although satisfactory short-term results are often achieved through surgical intervention (up to 80% of dogs improve), lesions redevelop in a high proportion (50% to 90%) of affected dogs, with complications including fecal incontinence or rectal stricture.

Perianal sinuses reportedly respond to immunosuppressive treatment protocols, which supports the hypothesis that the disease is immune mediated. Administration of prednisone at a high dose (2 mg/kg [0.91 mg/lb], PO, q 24 h for 2 weeks, followed by 1 mg/kg [0.45 mg/lb], PO, q 24 h for 4 weeks) and feeding of a novel-protein diet (ie, diet including protein to
which dogs had not previously been exposed) resulted in short-term improvement or cure in 67% of dogs with perianal sinuses and concurrent colitis in 1 study.13 Oral administration of cyclosporine, an immunosuppressant drug that inhibits T-cell activation and suppresses cell-mediated immune responses,36 yields even more remarkable short-term results than prednisone (up to 100% of affected dogs have an improvement in clinical signs, and 80% to 90% have resolution of lesions) but less successful long-term results (lesions redevelop in 30% to 50% of affected dogs).15-18,20,21

The main concern with treatment protocols that include cyclosporine is the high cost to owners. Other factors that may discourage use include logistic difficulties in measuring 12-hour trough (lowest) blood concentrations of cyclosporine and occasional adverse effects (eg, vomiting, diarrhea, oral growths, coat shedding, and hirsutism).15,17,40,41 To reduce the dose of cyclosporine without loss of efficacy, ketoconazole, which inhibits the hepatic metabolism of cyclosporine, can be concurrently administered.22,31-33 This approach may reduce cost to owners, although the cost and systemic effects of ketoconazole can be substantial. To further reduce treatment costs, protocols involving short-term administration of immunosuppressive drugs immediately prior to surgical intervention or administration of azathioprine have also been used but appear to be less effective.17,19,45-47

Tacrolimus (FK506) is a nonsteroidal immunomodulator with a mechanism of action that is similar to but much more potent than cyclosporine, although tacrolimus is structurally quite different. Tacrolimus is more efficacious when applied topically than cyclosporine, probably because of its much smaller molecular weight.46-50 Topical application of tacrolimus ointment yields considerable benefits in humans with psoriasis, atopic dermatitis, pyoderma gangrenosum, oral and perineal Crohn’s disease, and vulvar lichen sclerosis.31-34 It is also safe when applied topically for up to 1 year in humans, with minimal adverse effects and no evidence of systemic accumulation.35 Tacrolimus ointment is commercially available in 2 strengths, 0.1% and 0.03% (pediatric), and contains a base of mineral oil, paraffin, propylene carbonate, white petrolatum, and white wax.4 The product is sold via prescription in 30-, 60-, and 100-g tubes.4

The effect of topical application of 0.1% tacrolimus ointment as the sole treatment for perianal sinuses was evaluated in 10 dogs that were treated for 16 weeks.46 In that study, 5 dogs had complete resolution of lesions, 4 dogs had a partial response, and 1 dog did not improve. To our knowledge, there have been no additional reports of studies involving topical application of tacrolimus ointment in dogs with perianal sinuses. Lack of long-term follow-up in most studies makes it difficult to evaluate the long-term outcome of treatments for perianal sinuses.

The purpose of the study reported here was to evaluate responses to a 16-week treatment protocol consisting of twice-daily topical application of 0.1% tacrolimus ointment, a tapering dose of orally administered prednisone, a novel-protein diet, and short-term oral administration of metronidazole in dogs with perianal sinuses. We also sought to obtain information on the dogs’ lesion status at regular intervals for an additional 2 years. We hypothesized that results equivalent or superior to those of cyclosporine-based treatment protocols would be obtained, with minimal morbidity and considerable cost savings to owners.

Materials and Methods

Animals—Dogs with perianal sinuses evaluated at the Veterinary Teaching Hospital of the College of Veterinary Medicine, Michigan State University, from October 2002 through December 2005, were eligible for inclusion. Owner consent was obtained prior to enrollment, and participating owners agreed to allow regular and long-term follow-up of their dog’s lesion status for 2 years. Enrolled dogs were taken off all medication for perianal sinuses 2 weeks before the study began to allow any systemic medications to leave the bloodstream.

The following information was obtained for enrolled dogs: breed, age, sex, body weight, body condition score (9-point scale, with 1 indicating emaciation and 9 indicating obesity), history of weight loss, history of perianal sinuses, and presence of clinical signs of licking at the perineum, tenesmus or dyschezia, bleeding from the anal area, constipation, and diarrhea. Any previous treatments were recorded. A complete physical examination, CBC, and serum biochemical analysis were performed for each dog at the time of initial evaluation. Urinalyses were also performed. Dogs < 10 years of age routinely underwent 3-view thoracic radiography.

Evaluation of perianal sinuses—After initial evaluation, dogs were sedated with either acepromazine maleate (0.05 mg/kg [0.023 mg/lb], IV) and hydromorphone (0.07 mg/kg [0.032 mg/lb], IV) or medetomidine (10 to 40 µg/kg [4.5 to 18.2 µg/lb], IM). The perineum of each dog was clipped, cleansed with 0.05% chlorhexidine diacetate solution, and carefully examined with a probe. The anal sacs, external anal sphincter, and anorectal mucosa were closely inspected, and a digital rectal examination was performed to assess sphincter function and degree of thickening in the distal aspect of the rectum and anus. The perianal sinuses were assessed for maximal depth of the lesions and degrees of circumferential, anal sac, and rectal involvement. Degree of circumferential involvement was categorized as 0° to 90°, 90° to 180°, 180° to 270°, or 270° to 360°. Maximum depth was categorized as mild (<1 cm), moderate (1 to 2 cm), or severe (>2 cm). All perianal sinuses were photographed with a high-resolution digital camera.

Treatment protocol and assessment—All dogs were treated in accordance with a 16-week protocol consisting of the following treatments: topical application of 0.1% tacrolimus ointment on the perianal region, twice per day; oral administration of prednisone (2 mg/kg, q 12 h for 2 weeks; 1 mg/kg, q 24 h for 4 weeks; and then 1 mg/kg, q 48 h for 10 weeks); oral administration of metronidazole (10 mg/kg, q 12 h for 2 weeks); and local softener (eg, psyllium-based product or canned pumpkin) as needed. During the 16-week period, the diet of all dogs was restricted to a novel-protein diet (eg, veni-
son or fish and potato). The only allowable snacks were potatoes, apples, and carrots, and heartworm medication could not include meat flavoring.

Owners were asked to notice and record the time (in days) of any change in clinical signs and time (in days) of any change in lesion appearance. Dogs were reexamined every 4 weeks, lesions were photographed, and lesion changes were recorded. For those dogs with anal sac involvement, anal sacculectomy was recommended at that time. If approved by the owner, involved anal sacs were excised via an open technique and submitted for histologic evaluation. After the 16-week treatment concluded, owners were contacted for information on their dog's status every 6 to 12 weeks by telephone or in person during a follow-up appointment. When the 2-year period ended, the perineum of each dog was reexamined.

**Results**

**Animals**—Nineteen dogs were enrolled in the study. The mean age was 7.2 years (range, 1.5 to 12 years), and mean body weight was 36.4 kg (80 lb; range, 30 to 42.8 kg [66 to 94 lb]). The mean body condition score was 3.8 (range, 2 to 6), and 9 dogs had a history of weight loss associated with the onset of signs of perianal sinuses. Seventeen dogs were German Shepherd Dogs, 1 was a Chesapeake Bay Retriever, and 1 was an Irish Setter. Over the same period as this study, 4% of dogs admitted to the teaching hospital were German Shepherd Dogs. Ten of the study dogs were castrated males, 5 were spayed females, 2 were sexually intact males, and 2 were sexually intact females. For all dogs evaluated at the hospital during the study period, the ratio of castrated male to castrated female dogs was 0.9:1 and 32% were sexually intact.

Most of the 19 dogs had undergone treatment for perianal sinuses with various combinations of the following treatments: antimicrobial other than sulfasalazine (n = 10 dogs), prednisone or prednisolone (7), hypoallergenic diet (6), cyclosporine (3; 1 dog received an inadequate dose), sulfasalazine (2), surgery (2), and topically applied antimicrobial ointment (1) or antiseptic solution (1). In addition, once-daily topical application of 0.1% tacrolimus ointment (an inadequate dosing interval) had been prescribed for 1 dog treated with no other medication. Owners were all seeking treatment for their dog's condition because of a lack of response to these previous treatments. No dogs had received medication for perianal sinuses in the 2 weeks immediately before the study began. Dogs had a history of perianal sinuses that ranged from 1 month to 7 years.

No dog was free of clinical signs of perianal sinuses when initially evaluated at the hospital. Clinical signs at that time included licking at the anus (n = 17 dogs), tenesmus or dyschezia (13), bleeding from the anus (8), constipation (7), and diarrhea (7). In addition, 2 dogs were coprophagic, 1 dog ran while defecating, and another dog defecated inappropriately in secluded areas of the house. In 5 dogs, the only clinical sign was licking. Physical examination findings and clinical signs not associated with perianal sinuses included chronic superficial keratitis (pannus; 4), other ocular disease (5), dental tartar (1), lipoma (1), degenerative myelopathy (1), and arthritis (1). Five dogs had dry or scaly skin, a history of pruritic episodes, and alopecia.

Results of a CBC were unremarkable in 11 of 19 dogs; the remainder had a mild, mature neutrophilia (> 7.8×10^9/L), with variable mild monocytosis (> 0.7×10^9/L). Results of serum biochemical analyses were within reference ranges for 9 dogs; 8 dogs had a serum globulin concentration that slightly exceeded the upper reference limit of 4.1 g/dL. A urinalysis was performed for 16 dogs, and results were all within reference limits. The 3 dogs for which a urinalysis was not performed were < 4 years of age.

**Results of initial evaluation**—Results of digital rectal examinations at the initial evaluation, after 16 weeks of treatment, and 2 years later were summarized (Table 1). No rectocutaneous fistulae were detected during the initial digital rectal examination of any dog. One dog had roughened mucosa on the ventral rectum, and 3 dogs had a functional anal stenosis (swelling of the anal sphincter and perianal tissues without fibrosis). Sixteen of the 19 dogs resented rectal examination. Overall, 1 or both anal sacs were involved in the perianal sinuses in 9 dogs.

**Evaluation after the 16-week treatment**—All dogs completed the 16-week treatment protocol. Owners reported mean interval to improvement in clinical signs of 7 days (range, 4 to 14 days); 1 owner was unsure of the interval. The mean interval to improvement in lesion appearance was 13 days (range, 7 to 21 days). All owners reported improvement in clinical signs and lesion appearance; none reported deterioration in clinical signs or exacerbation of the lesions. A marked reduction in the frequency of coprophagia or inappropriate defecation was also reported for both coprophagic dogs as well as the inappropriately defecating dog.

Direct inspection and digital rectal examination revealed that perianal sinuses had completely resolved in 15 dogs, including the 5 dogs that underwent anal sacculectomy (Figure 1). Histologic evaluation of the anal sac tissue obtained from the dogs that underwent anal sacculectomy revealed evidence of moderate to marked chronic inflammatory responses, multifocal epithelial or subepithelial degeneration associated with mononuclear inflammatory cells, and varying degrees of fibrosis. In 4 dogs, perianal sinuses had partially resolved (Figure 2). Of these dogs, 3 had anal sac involvement but owners had declined anal sacculectomy for their dog because of considerable improvement in lesions and complete resolution of clinical signs. For the remaining dog with partially resolved lesions, the owner admitted poor compliance with the treatment protocol because of the nature of the dog. All 4 dogs with partially resolved lesions were fed the same commercial diet, and owners claimed complete compliance with the dietary component of the treatment protocol.

None of the adverse treatment effects reported by owners appeared to be associated with the tacrolimus ointment. Several owners reported signs that were consistent with and attributed to the high dose of oral prednisone during the first month of the protocol. These reported signs consisted of polyphagia, polydipsia, polyuria, and restlessness, all of which attenuated as the dose of prednisone was reduced. Owners reported that one 30-g tube of 0.1% tacrolimus ointment would
last for approximately 5 weeks with twice-daily application to the affected area. At our hospital, the cost of this medication to the owner for the 16-week period (4 tubes) was $484.

Assessment at 2 years—Three dogs died from causes unrelated to the perianal sinuses before the end of the 2-year follow-up period, and 1 dog was lost to follow-up. Of the 15 dogs available for follow-up at 2 years, all were

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**Table 1—Characteristics of perianal sinuses in 19 dogs at initial evaluation, after treatment in accordance with a 16-week protocol,* and after subsequent long-term (2-year) treatment with variations on the protocol.**

<table>
<thead>
<tr>
<th>Anal sac affected</th>
<th>Circum (°)</th>
<th>Maximum depth (cm)</th>
<th>Status at 16 weeks</th>
<th>Status at 2 years</th>
<th>Dosage of tacrolimus</th>
<th>Dosage of prednisone</th>
<th>Novel diet</th>
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<tr>
<td>A</td>
<td>None</td>
<td>360</td>
<td>1–2</td>
<td>CR</td>
<td>Dead†</td>
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<td>1–2</td>
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<td>None</td>
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*The treatment protocol included twice daily topical application of 0.1% tacrolimus on the perianal region, a tapering dose of orally administered prednisone, a novel-protein diet, and short-term (2 weeks) oral administration of metronidazole. †The cause of death was not related to perianal sinuses. ‡Dog had both anal sacs surgically removed 4 weeks after the initial evaluation. §Perianal sinuses would redevelop at 3 o’clock and 9 o’clock positions whenever the owner ceased applying the tacrolimus ointment. ||Owner admitted poor compliance with protocol. ¶Dog had intermittent anal erythema and, when the erythema was evident, received twice-daily topical application of 0.1% tacrolimus ointment and 10 mg of prednisone every other day until the erythema subsided.

Circum = Circumference. CR = Completely resolved. NA = Not available. PR = Partially resolved. PPF = Pinpoint fistulae. — = Drug not administered.
free of clinical signs of perianal sinuses. Thirteen of the 15 were still free of perianal sinuses lesions. The remaining 2 dogs still had tiny (pinpoint) fistulae over the anal sacs. Both owners had persistently declined anal sacculectomy because of the absence of any clinical signs.

The study recommendation was to discontinue all medications other than the novel-protein diet when the 16-week treatment concluded. Owners were not compliant with this recommendation and continued to medicate their dogs intermittently with 0.1% tacrolimus ointment (n = 11) and prednisone (4; Table 1). Of the 4 dogs that continued to receive prednisone, 2 still had tiny fistulae over the anal sacs, 1 was prone to recurrence of small lesions over the anal sacs (these lesions would resolve when 0.1% tacrolimus ointment was applied daily and 10 mg/kg prednisone was administered every other day), and 1 had firmer feces and ate better when receiving 5 mg of prednisone every other day, as reported by the owner. One dog was not maintained on the protocol medication; the dog's lesions had resolved completely during the 16-week treatment period, but it continued to have intermittent episodes of anal erythema. When these episodes happened, the owner would treat the dog with application of 0.1% tacrolimus ointment twice daily and 10 mg of prednisone every other day until the erythema subsided.

Eleven dogs continued to be fed a novel-protein diet during the 2-year period, whereas the remaining dogs returned to regular commercial pet food. The 2 dogs with residual pinpoint fistulae over the anal sacs had remained on a novel-protein diet; although complete owner compliance with respect to snacks could not be assured with one of the owners. Of the initial 9 dogs with a history of weight loss associated with the onset of perianal sinuses, 6 were available for the 2-year assessment. All 6 dogs had returned to what the owners considered a normal body weight.

Discussion

Distributions of breed, age, and sex in the present study of dogs with perianal sinuses were consistent with those of other reports,3,4,13,16,20–22,30,43 with German Shepherd Dogs being overrepresented and male sex predominating. The distribution of sexually intact dogs with perianal sinuses was slightly lower than that of our general hospital population during the same period; however, because of the limited number of dogs in the study, no conclusions can be made about this finding. Clinical signs, history, and physical examination findings associated with the perianal sinuses were consistent with those of other reports,24,28,39,62 including the weight loss that was evident in almost half (9/19) of the study dogs.

As our understanding of perianal sinuses grows, it is clear that immunosuppressive medication, specifically that which suppresses T-lymphocyte activation, should be the major component of any treatment protocol.3,6–9,23 Topical application of tacrolimus ointment reportedly inhibits T-lymphocyte activation and cytokine elaboration in the skin and draining lymph nodes.63 Unlike cyclosporine, which is most effective when administered orally, tacrolimus is effective topically, minimizing the risk of systemic adverse effects.50

Dogs with perianal sinuses may also have colitis.6,13 Clinical signs associated with colitis and perianal sinuses are similar (tenesmus, dyschezia, and hematochezia), and without histologic evaluation of colonic biopsy specimens, it was impossible to be certain whether clinical signs were compounded by the existence of concurrent colitis. Our intent was to develop a protocol to treat perianal sinuses and presumed concurrent colitis. The protocol developed was identical to the long-standing cyclosporine protocol used in our hospital, but in place of oral administration of cyclosporine, we...
substituted topical application of 0.1% tacrolimus ointment. The purpose of the tacrolimus was to inhibit T-lymphocyte activation, and that of the prednisone was to provide initial systemic immunosuppression; both drugs were intended to ameliorate lesions and signs associated with perianal sinuses. The 16-week protocol used also included metronidazole for the first 2 weeks. Metronidazole is an effective against anaerobic bacteria and protozoa and has some inhibitory action on cell-mediated immunity; it is commonly used to treat colitis in dogs. Finally, a strict novel-protein diet was included with the intent of allergen avoidance in the event that any concurrent colitis or the perianal sinuses may have been caused or exacerbated by a dietary antigen.

The rapid amelioration of clinical signs and improved appearance of perianal sinuses lesions in all dogs in the present study were encouraging. The combination of the tacrolimus ointment and prednisone appeared to control discomfort associated with defecation early during the treatment period. It is also possible that metronidazole treatment aided in reducing colonic irritation during the first 2 weeks. Adverse effects were transient (within the first month of the protocol) and were attributed to the high dose of prednisone because they resolved as the dose of prednisone was reduced.

The protocol used in the present study was effective at resolving or reducing perianal sinuses and associated clinical signs in all dogs, with most having complete resolution of their lesions. These results were similar to or better than responses obtained in other studies, in which orally administered cyclosporine was used as the sole treatment modality. In those studies, the proportion of dogs in which lesions resolved ranged from 69% to 100%. We could not determine whether the tacrolimus ointment, prednisone, or novel-protein diet was responsible for continued improvement during the 16-week study period. However, in another study, only 33% of dogs had complete resolution of their perianal sinuses when they received a high dose of prednisone and an alternative protein diet alone. This implies that the tacrolimus ointment was a critical component of the protocol in the present study. Only 1 study has been reported in which topically applied 0.1% tacrolimus ointment was used for the treatment of perianal sinuses in dogs. In that study, the lesions of 9 of 10 dogs noticeably improved, with those of 5 dogs healing fully.

Involvement of the anal sacs appeared to impede complete resolution of perianal sinuses in the dogs in the present study. Lesions in the 5 dogs with anal sac involvement that underwent anal sacculectomy all healed completely during the 16-week treatment period. Of the 4 dogs with anal sac involvement that did not have an anal sacculectomy, only 1 had complete resolution during the same period. These findings underscore the importance of thorough examination of the affected anal area at the time of initial examination and recommendation of anal sacculectomy should anal sacs be involved in the perianal sinuses. The anal sacs of German Shepherd Dogs are located deeper within the perianal tissue, and they extend further cranially into the external anal sphincter than in other breeds. Therefore, a meticulous technique and good anatomic knowledge are needed to ensure complete anal sacculectomy in German Shepherd Dogs, with minimal adverse sequelae.

In humans with oral and perineal Crohn’s disease, a mild stinging sensation after topical application of tacrolimus ointment is possible. None of the dog owners in the present study reported a behavior in their dog that could be attributed to irritation when the ointment was applied, but it should be mentioned that our protocol does require that the dog’s nature tolerate twice-daily topical application to the sensitive anal area. Discomfort associated with the perianal sinuses appeared to improve in the first week of treatment, and this relief of discomfort should facilitate topical application to the perineum.

A major advantage of the treatment protocol reported here is the considerable cost savings, compared with a similar protocol that includes cyclosporine. At our hospital, the cost of the 0.1% tacrolimus ointment for the 16-week treatment period (four 30-g tubes) was $484. On the other hand, the cost of cyclosporine (at 5 mg/kg [2.3 mg/lb], PO, q 12 h) for the 16-week protocol is between $2,326 and $2,417, depending on the weight of the dog. This does not take into account the cost of blood collection and laboratory fees that would be incurred during determination of the optimal dose of cyclosporine.

When cyclosporine is used as the immunomodulating agent in a treatment protocol, perianal sinuses can reportedly redevelop after treatment ceases, requiring additional cyclosporine treatment and often anal sacculectomy. We were unable to make conclusions about redevelopment of lesions in the dogs in our study because treatment was continued in all dogs with a reduced frequency of topical application of the tacrolimus ointment, with or without a low dose of prednisone and a novel-protein diet. The role of a specific novel-protein diet or the effect of increased dietary fish oils could not be ascertained because different diets were used and only 15 dogs were available for long-term assessment.

The 16-week treatment protocol used in the study reported here appeared effective at resolving perianal sinuses in dogs. Continuing treatment with 0.1% tacrolimus ointment at a lower frequency of application and with prednisone at a lower dose and frequency of administration appeared to control the disease for at least 2 years. No adverse effects associated with the tacrolimus ointment were reported during the whole study period. Anal sac involvement appeared to impede healing of the lesions, and anal sacculectomy should be considered for these situations. A substantial cost saving to owners can be achieved with this protocol, compared with the cost of protocols that involve cyclosporine. Additional prospective studies of perianal sinuses should be undertaken to compare the effects of protocols involving orally administered cyclosporine and topically applied tacrolimus ointment, ascertain the importance of specific novel-protein diets in these protocols, evaluate the potential role of dietary fish oils, and evaluate the effects of other T-cell inhibitors such as pimecrolimus.

b. Nikon Coolpix 4500, Nikon ring flash, Nikon Inc, Melville, NY.
c. Fish and Potato Canine Dry Formula, The Iams Co, Dayton, Ohio.
References


Selected abstract for JAVMA readers from the American Journal of Veterinary Research

**Effect of intravenous administration of tramadol hydrochloride on the minimum alveolar concentration of isoflurane in rabbits**

Christine M. Egger et al

**Objective**—To evaluate the effect of IV administration of tramadol hydrochloride on the minimum alveolar concentration of isoflurane (ISOMAC) that prevented purposeful movement of rabbits in response to a noxious stimulus.

**Animals**—Six 6- to 12-month-old female New Zealand White rabbits.

**Procedures**—Anesthesia was induced and maintained with isoflurane in oxygen. A baseline ISOMAC was determined by clamping a pedal digit with sponge forceps until gross purposeful movement was detected or a period of 60 seconds elapsed. Subsequently, tramadol (4.4 mg/kg) was administered IV and the posttreatment ISOMAC (ISOMAC<sub>T</sub>) was measured.

**Results**—Mean ± SD ISOMAC and ISOMAC<sub>T</sub> values were 2.33 ± 0.13% and 2.12 ± 0.17%, respectively. The ISOMAC value decreased by 9 ± 4% after tramadol was administered. Plasma tramadol and its major metabolite (M1) concentrations at the time of ISOMAC<sub>T</sub> determination varied widely (ranges, 181 to 636 ng/mL and 32 to 61 ng/mL, respectively). Intervals to determination of ISOMAC<sub>T</sub> and plasma tramadol and M1 concentrations were not correlated with percentage change in the ISOMAC. Heart rate decreased significantly immediately after tramadol administration but by 10 minutes afterward was not different from the pretreatment value. Systolic arterial blood pressure decreased to approximately 60 mm Hg for approximately 5 minutes in 3 rabbits after tramadol administration. No adverse effects were detected.

**Conclusions and Clinical Relevance**—As administered, tramadol had a significant but clinically unimportant effect on the ISOMAC in rabbits. Higher doses of tramadol may provide clinically important reductions but may result in a greater degree of cardiovascular depression. (*Am J Vet Res* 2009;70:945–949)

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