Get It For Me Pull Slip

Request Date: 9/19/2012 12:55:27 AM

Journal Title: Proceedings: making waves in Monterey: 23rd annual conference & expo

Volume:  
Issue:  
Month/Year: Aug 2002

Article Author: Dahlhausen B, Aldred S, 
Article Title: Resolution of clinical proventricular dilatation disease by cyclooxygenase 2 inhibition

Pages: 9-12

Location: MSL Book Stacks
Call Number: SF 994 A849 2002p

*UPDATE LOAN SOME DOC:

Customer Information: yourpetsfriend@gmail.com

Copyright Notice: This material may be protected by Copyright law (Title 17 U.S. Code)

Unable to pull because: (initial & date)

1. Volume Not On Shelf
2. Title Not On Shelf
3. Not Found As Cited/Other

**Bring item down & place in Borrowing Problem Box in room 142.

THIS REQUEST HAS BEEN FILLED BY:

OCLC: TMV
DOCLINE: TXUTAM
Medical Sciences Library
Texas A&M University

Phone: 979.845.7428
Fax: 979.845.0923
Email: docdel@library.tamu.edu
Ariel: 165.91.58.23
Odyssey: 165.91.74.104

NOTICE:
THIS MATERIAL MAY BE PROTECTED BY UNITED STATES COPYRIGHT LAW (TITLE 17, U.S.C)

REQUESTING RESEND:

We prefer E-mail, but will accept by phone, fax, or Ariel

| THIS IS NOT AN INVOICE | 

(any charges will be invoiced separately at the end of the billing quarter)
Resolution of Clinical Proventricular Dilatation Disease by Cyclooxygenase 2 Inhibition

Bob Dahlhausen DVM, MS, Steve Aldred MD, Dipl ACP, and Ernie Colaizzi

Session #1030

Affiliation: From Research Associates Laboratory, Inc., 14556 Midway Rd., Dallas, TX 75244, USA.

Abstract: Proventricular dilatation disease is a lymphocytic, plasmacytic ganglioneuritis and myositis of pet birds. The disease is usually fatal with no known treatment. Selective inhibition of cyclo-oxygenase-2 by celecoxib has proven safe and effective in reducing the clinical pathology of this disease and leads to improved physical status and survivability in affected birds.

Proventricular Dilatation Disease

Proventricular dilatation disease (PDD) is a fatal disease of pet birds characterized by a lymphocytic, plasmacytic infiltrate of central (CNS) and peripheral nerve tissues. Myenteric plexuses supplying the digestive tract are commonly affected, causing atrophy of the smooth muscles of the crop, proventriculus, ventriculus, or small intestine. Gastrointestinal motility disorders and various degrees of organ dilatation develop. Affected birds may exhibit progressive weight loss, regurgitation, crop impaction, and passage of undigested food. Secondary bacterial and fungal infections are commonly observed. With CNS involvement, birds may exhibit a lack of coordination, ataxia, and motor and proprioceptive deficits. Some may show only CNS signs, lacking typical digestive tract involvement. Conduction pathways in the heart may also be affected causing acute death in an otherwise normal appearing individual.

Clinical laboratory findings in PDD are inconsistent. A presumptive diagnosis is based upon the history, clinical signs, and radiographic evaluation of the digestive tract. Diagnosis can be confirmed by demonstrating the characteristic histopathologic lesions in tissues from affected birds. While supportive care may help to prolong the lives of birds with PDD, there is no current treatment for this disease. Historically, long-term prognosis is grave with a mortality figure approximating 100%. Most birds succumb within a 1-year period to progressive debilitation, secondary infections, or CNS disturbances. The reader is referred to the paper by Gregory for further review of this disease.

Rationale for therapy

The ganglioneuritis and encephalomyelitis associated with PDD is inflammatory in nature. It is characteristic of an inflammatory response to a viral agent. A viral-induced autoimmune response has even been suggested as the underlying cause of this disease. The chronicity of this process contributes to the progressive, debilitating nature of the disease. Diminishing this reaction was expected to lead to clinical improvement and possible resolution of clinical signs in affected birds. Anecdotal reports suggest improved clinical status in birds treated with steroidal anti-inflammatory agents. The risks associated with the use of these agents in avian species make them an inappropriate choice for long term treatment consideration. Anti-inflammatory agents with significant activity in...
the CNS, peripheral nervous system, and gastrointestinal tract that would be safe for use in pet birds were investigated. Of these, the non-steroidal anti-inflammatory drugs (NSAIDs) appeared most useful.

NSAIDs, through inhibition of the cyclooxygenase (COX) enzyme, are effective for relief of inflammatory processes. COX exists in at least 2 isoenzyme forms: COX-1 and COX-2. The first, COX-1, is expressed in most tissues where it converts arachidonate to the prostaglandins involved in normal homeostatic cell activity. The second, COX-2, is an inducible form that is present in immune cells, endothelial cells of the vascular system, and synovial fibroblasts. It causes enhanced formation of prostaglandins that are involved in acute and chronic inflammatory processes. Conventional NSAIDs inhibit both COX-1 and COX-2 enzymes. Their long-term use is tempered by the development of toxic side effects from COX-1 inhibition. The primarily involve platelet function, renal function, and gastrointestinal tract cytoprotection.

**Celecoxib**

Celecoxib (Celebrex, Pfizer, Groton, CT, USA), part of a new family of NSAIDs, is a potent and selective inhibitor of the COX-2 isoenzyme. It is the first specific inhibitor of COX-2 approved for use in the United States. Specific inhibition of the COX-2 isoenzyme has been shown to effectively reduce many parameters of inflammation including edema, white blood cell infiltration, and white blood cell activation. At therapeutic levels, celecoxib does not affect the normal homeostatic function of COX-1.

Approved for use in osteoarthritis, celecoxib also has potent anti-inflammatory activity in the gastrointestinal tract. In patients with intestinal adenomatous polyposis, celecoxib leads to a significant reduction in the number of colorectal polyps, thereby decreasing the risk of colorectal cancer. In animal models of colon, skin, breast, prostate, and urinary bladder cancer, celecoxib has significant antineoplastic and anticarcinogenic activity. It is of interest to note that celecoxib has also been shown to inhibit certain CNS viruses both in vitro and in vivo.

After oral administration, celecoxib is widely distributed, with highest concentrations in the gastrointestinal tract. It circulates almost exclusively bound to plasma albumin. Celecoxib is metabolized primarily by hepatic microsomes (cytochrome P450) to carboxylic acid and glucuronide metabolites. The major route of excretion in most species is via the feces, with the remainder excreted in the urine. The elimination half-life is about 11 hours.

Celecoxib has significant tolerability and safety advantages compared with the non-selective NSAIDs. In human long-term administration (q12h x 2 yrs), the incidence of adverse events was similar to placebo groups in most instances.

**Therapeutic protocol**

Celecoxib (10 mg/kg orally, q24h) was used for the management of birds with clinical PDD. Diagnosis was based upon history, physical and radiographic exam, and characteristic crop biopsy pathology. The drug was made into an aqueous suspension (10 mg/ml), kept refrigerated, and replaced every 14 days. Treatment duration was for a period of 6–24 weeks with the decision to cease medication based upon the return to normal body weight, condition, and diet. Contrast radiography was also used to monitor the progression of clinical improvement.

Supportive care to improve gastrointestinal transit (fluids, apple pectin), nutritional support with easily digested feeding formulas, and appropriate therapy to eliminate bacterial and fungal enteric infections were administered as needed. Improvement in clinical condition was generally observed within the first 7–14 days of treatment. A gradual resolution of clinical signs and return to normal body condition occurred over the course of therapy. Periodic monitoring of clinical hematology and serum chemistry profiles did not demonstrate any adverse effects related to this extended therapy. The majority of birds treated demonstrated marked clinical improvement including
those in advanced stages of the disease. Most treated birds maintained their improved clinical status after treatment cessation. However, premature cessation of treatment can result in recrudescence of clinical signs. In these instances, clinical improvement resumed with additional medical therapy.

Treatment success was best in birds with early diagnosis and before the disease had severely advanced. Some severely debilitated individuals had such advanced disease that they did not survive through the initial stages of therapy or improved, but did not regain complete normalcy. To date, over 14 affected birds had been treated. Most all have shown marked clinical improvement and are alive today. Many have regained a normal physical status. The longest survivor, a 6-year-old blue and gold macaw (*Ara ararauna*), finished therapy over 2 years ago. The bird remains in normal physical condition on a normal diet of pellets, seeds, and mixed foods. Previous radiographic changes have resolved and the bird is now negative on crop biopsy for PDD pathology.

**Conclusion**

Celecoxib is useful for the management of PDD in pet birds. It significantly improves the functional status of PDD affected individuals and appears to be safe and well tolerated in these species. It improves physical status allowing for enhanced survivability from this disease. Practitioners are cautioned to avoid the concurrent use of fluconazole because clinically significant drug interactions have been documented; however, celecoxib does not appear to interact with ketoconazole.¹⁰

We are currently accumulating additional clinical data to further evaluate the safety and efficacy of celecoxib use in pet birds. Until such time when a particular etiologic agent of PDD can be identified and appropriate screening measures developed, the infectious status of treated/recovered individuals remains unknown. Strict isolation and sanitation of affected birds is recommended.

**Acknowledgments:** The author thanks the Midwest Avian Research Expo, Miami Valley Bird Club, Central Indiana Caged Bird Club, and Kentuckiana Bird Club for the support that made this research possible.

**References**


