Resolution of Clinical Proventricular Dilatation Disease by Cycloogenase 2 Inhibition

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This report highlights important research advancements into the cause and nature of Proventricular Dilatation Disease (Myenteric Ganglioneuritis, or Macaw Wasting Disease) in pet birds. The discovery of a suitable pharmacotherapy that allows for the reversal and resolution of clinical signs is significant and warrants its early dissemination. We have confirmed the effectiveness of this treatment in eight well-documented cases and have seen improvement in numerous other ongoing cases under therapy. It is the author's intent that applied clinical use will further define the guidelines for this approach and immediately benefit those veterinarians managing clinically affected patients.

Proventricular Dilatation Disease (PDD) is a fatal disease of birds characterized by a lymphocytic, plasmacytic inflammatory infiltrate of central (CNS) and peripheral nervous tissues. Nerve ganglia supplying the musculature of the digestive tract are frequently affected, causing atrophy of the smooth muscles of the crop, proventriculus, ventriculus, and/or small intestine resulting in motility disorders and various degrees of dilatation.. Progressive weight loss, regurgitation, crop impaction, passage of undigested food, and secondary enteric bacterial and fungal infections are commonly observed. Lack of coordination, ataxia, motor and proprioceptive deficits are often seen with CNS involvement. While supportive care may help prolong the lives of affected birds, there is no current treatment for this disease. Long-term prognosis is grave, with the majority of birds succumbing after a period of progressive debilitation and wasting.

PDD is a disease of suspected viral etiology with a potentially long incubation period of months to possibly years. Because the lesions of PDD are inflammatory in nature, we speculated that diminishing this reaction might lead to clinical improvement and resolution of clinical signs in affected birds. Anti-inflammatory agents with significant activity in the CNS, peripheral nervous system, and gastrointestinal tract that were safe for use in pet birds were identified. Of these, the non-steroidal anti-inflammatory drugs (NSAIDs) appeared most useful.

NSAIDs, through inhibition of the cycloogenase (COX) enzyme, are effective for relief of inflammatory processes. COX exists in at least two isoenzyme forms: COX-1 and COX-2. COX-1 synthesizes prostaglandins that are involved in the regulation of normal homeostatic cell activity including gastrointestinal tract cytoprotection. COX-2 is an inducible form that causes enhanced formation of prostaglandins involved in acute and chronic inflammation. Conventional NSAIDs inhibit both COX-1 and COX-2. Their use is tempered by the development of side effects from COX-1 inhibition, which primarily involve platelet function, renal function, and the gastrointestinal tract.

Celecoxib (Celebrex, Pfizer), part of a new family of NSAIDs, is a potent and selective inhibitor of the COX-2 isoenzyme. The specific inhibition of COX-2 has been shown to effectively reduce many parameters of inflammation, including edema, white blood cell infiltration, and activation. At therapeutic levels, it does not inhibit COX-1 and has been shown to be well tolerated and safe. The incidence of adverse events is similar to placebos in most instances. In addition to its use in osteoarthritis, celecoxib has potent anti-inflammatory and anti-neoplastic activity in the gastrointestinal tract and has also been shown to inhibit certain CNS viruses in vivo and in vitro.

We have used celecoxib at 10 mg/kg orally once daily for the treatment of birds with clinical PDD. Diagnosis was based on history, clinical exam, characteristic radiographic changes, and crop biopsy pathology. Treatment duration was for a period of 6 to 12 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. Premature cessation of treatment can result in the recrudescence of clinical signs. In these instances, clinical improvement resumed with additional medical therapy. Supportive care to improve gastrointestinal transit (fluids, apple pectin), nutritional support with easily digested hand-feeding formulas, and appropriate therapy to eliminate bacterial (Clostridial) and fungal enteric infections were utilized as needed. Improvement in clinical condition is generally observed within the first week of treatment with a gradual resolution of clinical signs and a return to normal diet over the course of therapy. Periodic monitoring of clinical hematology and serum chemistry profiles have not demonstrated any adverse side effects related to this extended therapy. No adverse effects were observed clinically either during or after cessation of treatment. 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. The longest we have observed is a Blue & Gold Macaw that finished therapy over 1.5 years ago.

We are currently accumulating additional clinical data to further evaluate the safety and efficacy of celecoxib use in pet birds. Our experience has shown that it significantly improves the functional status of PDD-affected birds, and appears to be safe and well tolerated in these species. Until such time when a particular agent that causes PDD is identified and a suitable diagnostic assay developed to identify infected individuals, the infectious status of treated/recovered individuals remains unknown. A detailed report with clinical case summaries has been submitted for presentation at the next AAV convention.

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