

Clinical Outcomes of Azodyl Administration in Three Dogs with Chronic Kidney Disease

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ABSTRACT

Three dogs with chronic kidney disease were treated with Azodyl for more than 1 year. Azodyl induced a significant improvement in appetite, as well as an increase in body weight, improvement in lethargy, and decrease in blood urea nitrogen and/or creatinine levels, allowing for the discontinuation of fluid therapy.

INTRODUCTION

Chronic kidney disease (CKD) is the most common disease diagnosed in dogs, with a prevalence of up to 25% at referral institutions.^{1,2} Significant clinical signs of CKD include weight loss, vomiting, and decreased appetite.³ There are several treatment options for dogs with CKD: medical management, dietary therapy, and fluid therapy. The purposes of the treatments are as follows:

- prevent renal function, minimize uremic toxin production, promote solute excretion via fluid diuresis
- counter anemia
- protect the gastrointestinal tract from secondary uremic injury, and

- provide calcium and phosphorus homeostasis.⁴⁻⁶

Recently, the ability of synbiotics to modulate the intestinal microbiota and reduce the progression of CKD has been investigated using *in vitro* and *in vivo* studies in animals and humans.⁷⁻¹⁰ Specific bacteria capable of metabolizing urea, creatinine, indoles, and nitrosamine into non-toxic metabolites have been used. Azodyl (Vetoquinol, Lure, France) is a synbiotic used in cats with CKD.¹¹ Azodyl contains strains of three naturally occurring bacteria, combined with a prebiotic, in an enteric-coated capsule that releases the contents within the ileo-colic region. Azodyl reportedly improved azotemia in nephrectomized rats.¹²

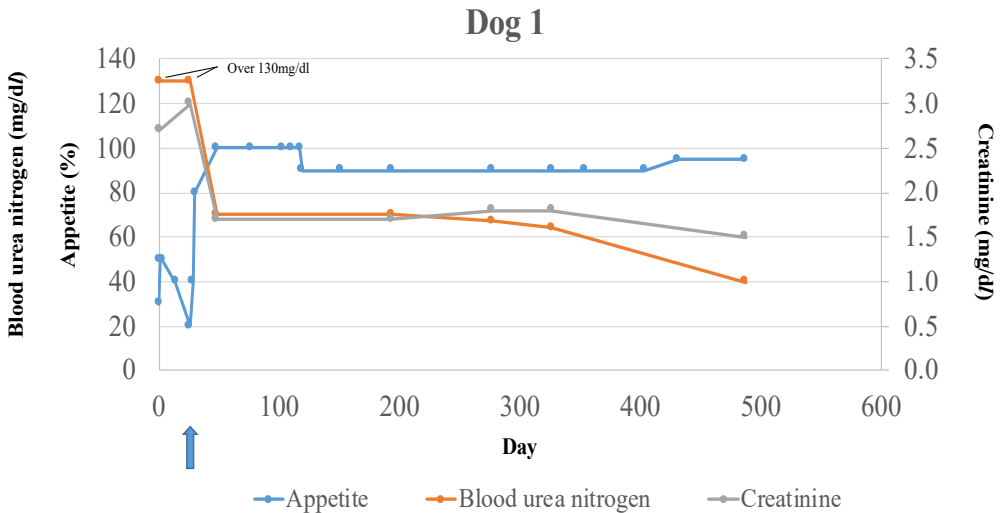
However, to the best of our knowledge, the efficacy of Azodyl in dogs with CKD has not been thoroughly investigated. This report describes the clinical outcomes in three dogs with CKD that were treated with Azodyl.

Case Descriptions

Case 1, a 13-year-old spayed female Maltese weighing 2.2 kg [body condition score (BCS) 2/9 and muscle condition score (MCS) moderate] was presented with a

Figure 1. Changes in appetite, along with blood urea nitrogen and creatinine levels, in Case 1.

Azodyl was initiated on the 26th day (arrow). The patient's appetite rapidly improved within several days, and blood urea nitrogen and creatinine levels decreased.



decreased appetite and lethargy of several months duration. The dog's normal body weight (BW) was 3.0 kg, and she had a 3-year history of Stage C chronic heart failure (CHF) caused by mitral valve disease (MVD), based on the American College of Veterinary Internal Medicine (ACVIM) consensus statement, that was controlled with pimobendan, alacepril, and furosemide. Physical examination revealed severe dehydration, and a Grade IV/VI left apical systolic heart murmur was auscultated. Clinical pathology revealed azotemia [blood urea nitrogen (BUN), >130 mg/dl; creatinine, 2.7 mg/dl] and an elevated serum phosphorus level (15.6 mg/dl).

We diagnosed the dog with Stage 3 CKD, based on the International Renal Interest Society (IRIS) staging guidelines. The dog received fluid therapy (100 ml SC q 48hr), Ipakitine, and metoclopramide, and furosemide was discontinued. Even after the fluid therapy was increased to 200 ml SC q48h, the patient's appetite did not improve, and the BW decreased to 1.8 kg. On the 26th day after diagnosis, Azodyl administration was initiated. On the 28th day, the patient's appetite was slightly improved, and, on the

30th day, the appetite was further improved, and the BW had increased to 2.0 kg. On the 48th day, the patient's appetite had returned to normal, and the amount of fluid therapy was reduced to 100 ml SC q 48hr. Clinical pathology revealed decreased BUN (70 mg/dl), creatinine (1.7 mg/dl), and serum phosphorus (4.5 mg/dl) levels. On the 76th day, the patient's BW had increased to 2.65 kg, the lethargy was improved, and fluid therapy was decreased to 100 ml SC q 72hr. On the 110th day, the appetite was normal, and fluid therapy was discontinued. On the 487th day, the dog showed no clinical signs, and the appetite was normal, although the BUN level remained mildly increased (40 mg/dl) (Figure 1).

Case 2, a 15-year-old castrated male Pomeranian weighing 4.6 kg (BCS 4/9 and MCS moderate) was presented with a decreased appetite, vomiting, polydipsia, and polyuria of several months duration. The patient's normal BW was 5.0 kg, and the dog had a history of gallbladder sludge and diabetes controlled with insulin.

Physical examination revealed moderate dehydration. Clinical pathology showed increased BUN (70 mg/dl) and creatinine

Figure 2. Changes in appetite, along with blood urea nitrogen and creatinine levels, in Case 2.

Azodyl was initiated on the 6th day (arrow). The patient's appetite rapidly improved within several days, and blood urea nitrogen level decreased.

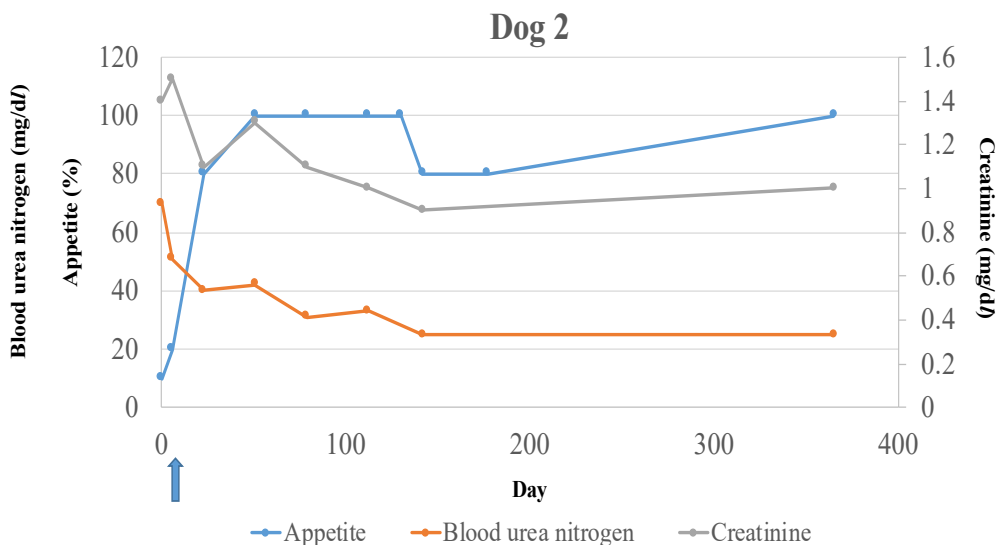
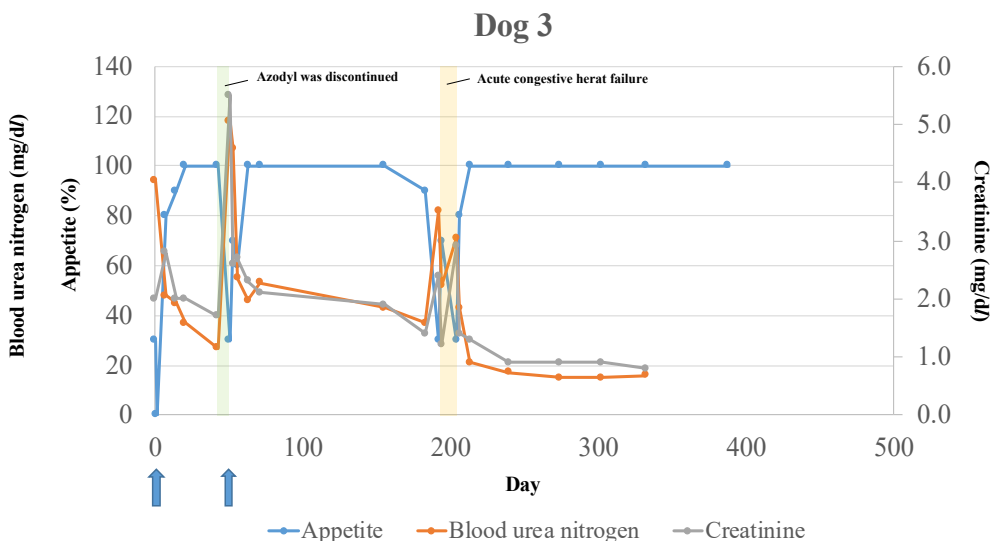


Figure 3. Changes in appetite, along with blood urea nitrogen and creatinine levels, in Case 3.

Azodyl was initiated on the 7th day, discontinued on the 42nd day, and restarted on the 50th day (arrow). The patient's appetite improved both times within several days of starting the medication. On the 192nd day, the dog developed acute heart failure and pulmonary edema. The blood urea nitrogen and creatinine level increased by administration of furosemide.



(1.5 mg/dl) levels, proteinuria [urinary protein:creatinine ratio (UPC), >8.0], and decreased urine specific gravity (USG) (1.010). We diagnosed the dog with Stage 2 CKD, based on the IRIS staging guidelines. The dog received fluid therapy (200 ml SC q 24hr). On the 6th day, the patient's appetite had not improved, although the BUN level had decreased (50 mg/dl). Therefore, Azodyl administration was initiated. On the 23rd day, the patient's appetite was improved, and the BW had increased to 4.9 kg. Fluid therapy was discontinued, and telmisartan was initiated. On the 365th day, the appetite remained normal, and the BUN level was decreased (Figure 2).

Case 3, a 12-year-old castrated male mixed breed dog weighing 6.26 kg (BCS 3/6 and MCS mild) was presented with decreased appetite, vomiting, polydipsia, and polyuria. The dog had a history of Stage B2 MVD, based on the ACVIM consensus statement. Physical examination revealed severe dehydration, and a Grade IV/VI left apical systolic heart murmur was auscultated. Clinical pathology revealed azotemia (BUN, 94 mg/dl; creatinine, 2.8 mg/dl) and an increased serum phosphorus level (11.3 mg/dl). We diagnosed the dog with Stage 3 CKD, based on the IRIS staging guidelines.

The dog received fluid therapy (250 ml SC q 24hr), Ipakitine, and metoclopramide. However, the appetite continued to decrease, so Azodyl administration was initiated. On the 42nd day, the patient's appetite was improved, the BW increased to 6.6 kg, and BUN and creatinine levels had decreased (27 mg/dl and 1.7 mg/dl, respectively). At the owner's request, the Azodyl was discontinued on 42nd day. However, on the 50th day, the patient's appetite again decreased, and BUN and creatinine levels increased (118 mg/dl and 5.5 mg/dl, respectively). The Azodyl was restarted on the 50th day, and the patient's appetite improved. On the 192nd day, the dog developed acute heart failure and pulmonary edema. The patient's appetite decreased, and the BUN and creatinine level increased by administration of fu-

roseamide. On the 204th day, the pulmonary edema and appetite had improved. On the 388th day, the dog showed no clinical signs, and the appetite remained normal (Figure 3).

DISCUSSION

The primary finding of this report is that Azodyl induced a significant improvement in appetite several days after the initial administration, along with increasing the BW and decreasing BUN and/or creatinine levels. It has been reported that survival times for CKD are associated with IRIS stage, BCS, MCS, BUN level, and UPC, and the median survival time for the cases presented is approximately 1 year, according to previous reports.^{3,13,14} However, the dogs under our Azodyl administration have been doing well for more than one year after the initial diagnosis.

Patients with CKD often exhibit some degree of anorexia, depending on the stage of CKD.¹⁵ In patients that are unwilling or unable to eat, nutrition may be provided by feeding tubes.¹⁶ Gastrostomy tubes appear to be safe and effective for improving the nutritional status of dogs with CKD.¹⁷ However, complications of feeding tubes include discharge, swelling, erythema, and pain, and replacement of the tubes is needed in some cases.¹⁷ The owners of the dogs in the above cases expressed a strong preference for Azodyl over feeding tubes and did not complain about the difficulty of administering the medication, even in the small breed dogs.

In dogs, MVD is common,¹⁸ and progression of MVD causes CHF.¹⁹ As shown in Cases 1 and 3, CKD and MVD can be concurrent. Martinelli et al. reported a 25% prevalence of CKD associated with azotemia in dogs with MVD.²⁰ In dogs with MVD, left ventricular and atrial functions are decreased.²¹ Fluid therapy is frequently administered for CKD; however, it can contribute to the occurrence of CHF in dogs with MVD.⁶ Therefore, veterinarians often debate the use of fluid therapy in dogs with MVD.

In our cases, especially Case 1, we also debated the use of fluid therapy because of

the medical history of CHF. However, fluid therapy was decreased in frequency and finally discontinued after the addition of Azodyl.

In this report, we described three cases that demonstrated positive clinical outcomes with the use of Azodyl. Therefore, Azodyl can be considered one of the options for therapy in dogs with CKD.

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