The Clinical Utility of a Hydrolyzed Renal Food in Managing Complex Feline Comorbidities

Clinical Evidence Review

Veterinary professionals are increasingly faced with cats presenting with concurrent chronic conditions, such as chronic kidney disease (CKD) alongside a food sensitivity manifesting as chronic enteropathy (CE). A growing body of scientific evidence supports the use of targeted nutritional interventions as an integral component of the management plan to address the complex pathophysiology of these concurrent diseases.

Hill's Prescription Diet k/d + z/d Hydrolyzed

THE THERAPEUTIC DILEMMA OF COMORBIDITIES

The management of feline CKD is frequently complicated by the presence of concurrent diseases. CKD is one of the most common diagnoses in feline practice, estimated to affect 1 in 3 cats in their lifetime.[1] The prevalence increases dramatically with age, affecting over 80% of cats 15 years or older.[2] This obstacle is common as data indicate approximately 1 in 5 cats with CKD also has a concurrent gastrointestinal or skin condition.[3] A particularly challenging scenario arises when a cat with a history of a food sensitivity develops CKD later in life. Studies show that feline chronic enteropathies — such as food-responsive enteropathy (FRE) and immunosuppressant-responsive enteropathy (IRE) — are often diagnosed in middle-aged cats.[4,5]

This chronological progression creates a significant therapeutic dilemma. A cat may have been successfully managed and stable for years on a hydrolyzed or novel protein food for their CE. When this stable patient is newly diagnosed with CKD, the veterinarian faces a difficult choice:

- **Maintain the current GI-focused therapeutic nutrition:** This approach avoids disrupting long-term GI stability but fails to provide the targeted renal support — such as controlled phosphorus and high-quality protein — supported by consensus guidelines from the iCatCare Veterinary Society, and foundational to the treatment approach of the International Renal Interest Society (IRIS).[6,7]
- **Transition to renal therapeutic nutrition:** This is the recommended approach for managing kidney health but introduces a substantial risk of triggering a relapse of GI signs as the intact proteins can provoke an adverse immune reaction.

This clinical crossroads forces a compromise where the nutritional strategy for one condition may come at the expense of the other, potentially jeopardizing the patient's overall health and quality of life. An integrated nutritional solution is needed.

FOUNDATIONAL EVIDENCE FOR NUTRITIONAL MANAGEMENT OF FELINE CKD

The clinical efficacy of the nutritional profile found in Prescription Diet k/d is supported by the highest level of clinical evidence. A 2-year, randomized, controlled clinical trial investigated this therapeutic nutrition in cats with spontaneous IRIS Stage 2 and 3 CKD.[8] The results demonstrated a profound impact on the most severe clinical outcomes. Cats consuming the nutrition of k/d experienced no uremic episodes (0%), whereas 26% of cats eating a typical maintenance food suffered a uremic crisis. *Figure 1.* Furthermore, there were no CKD-related deaths (0%) in the group fed the nutrition of k/d, compared to a 22% mortality rate in the control group.[8] *Figure 2.*

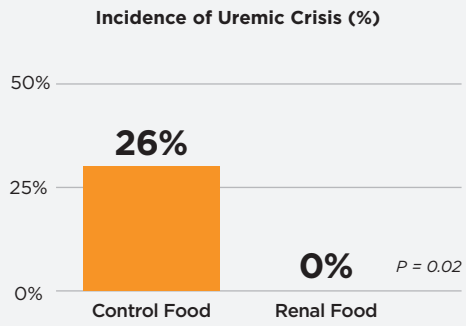

Figure 1. Percentage of cats that developed uremic crises while eating the renal food (nutrition of k/d) compared with the control food during the study period.

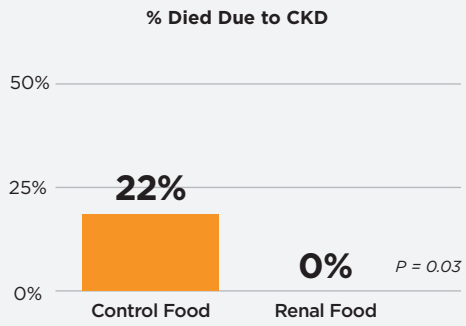

Figure 2. Percentage of cats that died secondary to CKD while eating the renal food (nutrition of k/d) compared with the control food during the study period.

A significant concern for clinicians managing feline CKD is patient inappetence. This poor appetite and insufficient caloric intake can exacerbate disease-associated cachexia and age-related sarcopenia, ultimately leading to a loss of body weight and/or muscle mass, which significantly impacts morbidity and survival.[9] A prospective, 6-month, randomized clinical trial directly addressed this, comparing the nutrition of k/d to a leading competitor's renal food in cats with IRIS Stage 1 and 2 CKD.[10] Cats consuming the competitor food lost significant body weight (-13.0%) and lean body mass (-11.1%). In stark contrast, cats fed the nutrition of k/d gained body weight (+5.8%) and, critically, maintained their lean muscle mass.[10] This superior outcome was attributed to a more optimal essential amino acid profile and enhanced palatability, resulting in a 23% greater voluntary caloric intake.[10] The high acceptance of the nutrition of k/d was further confirmed in a large-scale, real-world study that demonstrated a 94% successful transition rate.[11]

TARGETED SUPPORT FOR FOOD SENSITIVITIES WITH HYDROLYZED PROTEIN

The management of CE serves as a prime example of the clinical benefits of hydrolyzed protein. Hydrolysis breaks down proteins into small peptides and free amino acids, reducing their potential to trigger an adverse immune response.[12] This approach has proven effective; an observational cohort study utilizing anonymized veterinary clinical data to describe responses found that of 697 cats (71% of the total cohort) first prescribed a hydrolyzed diet as the sole initial therapy (without concurrent antibiotics or glucocorticoids) for chronic vomiting and/or diarrhea of undetermined etiology, 66% did not experience a poor response.[13] A poor response was defined as the subsequent prescription of antibiotics or glucocorticoids for vomiting/diarrhea, or death associated with GI

signs, during a median follow-up time of 818 days.[13] This was additionally supported by a prospective clinical trial in which eight cats with CE were fed an exclusive hydrolyzed protein food.[14] In this study, a complete resolution of clinical signs — based on the Feline Chronic Enteropathy Activity Index (FCEAI) — was observed in 100% of cats within 4 to 8 days, with significant improvements in scores for attitude, appetite, vomiting and diarrhea.[14]

Beyond its hypoallergenicity, hydrolyzed chicken protein offers two additional significant benefits directly supported by peer-reviewed research. First, it enhances palatability. A recent study utilized the industry-standard two-bowl preference test to compare foods formulated with hydrolyzed chicken liver against a control food with standard poultry byproduct meal.[12] The results showed that cats had a significant preference for the hydrolyzed chicken protein, consuming up to 2.8 times more of the hydrolyzed food than the control. This demonstrated preference is a critical advantage for encouraging food intake in chronically ill, often inappetent patients.

Second, the hydrolyzed protein positively influences the gut microbiome. The same study found that cats fed the hydrolyzed chicken food had higher fecal concentrations of beneficial short-chain fatty acids (SCFAs).[12] These SCFAs are essential for maintaining the health and integrity of the intestinal barrier, providing a direct, positive impact on the gut environment and a compelling link to the gut-kidney axis, a key pathway in the progression of CKD.

ADVANCED RENAL SUPPORT VIA THE GUT-KIDNEY AXIS

Recent evidence has established a definitive link between the gut microbiome and CKD progression, known as the "gut-kidney axis."[15] In feline CKD, gut dysbiosis leads to increased production of uremic toxins, like indoxyl sulfate (IS), which are absorbed into the bloodstream and can promote renal inflammation and fibrosis.[16-18] This evidence identifies the gut as a key therapeutic target. To investigate this target, ActivBiome+ Kidney Defense prebiotic blend and betaine were developed. A clinical study in cats with early-stage CKD evaluated a renal food supplemented with this proprietary blend of prebiotics and betaine. The study found this nutrition led to a significant reduction in multiple gut-derived uremic toxins.[19] This demonstrates a tangible, evidence-based mechanism for beneficially modulating the gut-kidney axis and managing a key driver of CKD progression. To apply this nutritional approach to patient management, ActivBiome+ Kidney Defense is included in Prescription Diet k/d + z/d feline.

Hill's ActivBiome+ Kidney Defense is a proprietary blend of betaine and prebiotics shown to activate the gut microbiome to help protect kidney function.

Ingredient	Site of Action	Description/Function
Betaine	Kidney	A nutrient that functions as an osmolyte to support cell hydration and has antioxidant & anti-inflammatory properties
Short-chain fructooligosaccharides (scFOS)	Proximal colon	Soluble, simple fiber that modulates the microbiome (proximal colon) and helps reduce uremic toxins produced by gut bacteria
Oat beta glucan	Distal colon	Soluble, complex fiber that modulates the microbiome (distal colon) and helps reduce uremic toxins produced by gut bacteria

A UNIFYING SOLUTION FOR CONCURRENT DISEASE

The evidence culminates in a compelling nutritional strategy for cats suffering from CKD with concurrent food sensitivities. A single integrated therapeutic nutrition like Prescription Diet k/d + z/d addresses these multiple conditions simultaneously:

- **For CKD:** It provides the clinically proven benefits of the nutrition of k/d — controlled phosphorus, high-quality protein and an optimal amino acid profile — to manage renal disease, slow its progression and support lean muscle mass.
- **For CE:** The hydrolyzed protein source minimizes the risk of triggering adverse immune reactions, helping to manage associated gastrointestinal signs.
- **For overall health:** The integration of ActivBiome+ Kidney Defense helps target the gut-kidney axis to reduce the production of harmful uremic toxins.

It is critical to note that this integrated approach cannot be replicated by simply mixing Prescription Diet k/d and Prescription Diet z/d feline together. Doing so would compromise the therapeutic integrity of both. Mixing dilutes the precise, evidence-based nutrient profile essential for renal care, failing to provide the full support needed to manage CKD. Simultaneously, it reintroduces intact proteins from the renal therapeutic food, destroying the hypoallergenic integrity of the hydrolyzed food and risking a relapse of gastrointestinal or dermatologic signs.

Prescription Diet k/d + z/d offers a unified, evidence-based nutritional solution for complex comorbid cases. This eliminates the therapeutic compromise, enabling veterinarians to provide comprehensive care that addresses the intricate pathophysiology of these challenging conditions.

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