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Nutritional Management of Chronic Renal Disease in Dogs and Cats

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Dietary therapy has remained the cornerstone of management of chronic renal failure for decades. The goals of dietary modification are to (1) meet the patient's nutrient and energy requirements, (2) alleviate clinical signs and consequences of the uremic intoxication, (3) minimize disturbances in fluid, electrolyte, vitamin, mineral, and acid–base balance, and (4) slow progression of the renal failure. Recommendations regarding dietary therapy and other components of conservative medical management must be individualized based on clinical and laboratory findings. Chronic renal failure is progressive and dynamic, and therefore serial clinical and laboratory assessment and modification of therapy in response to changes in the patient's condition are integral to successful therapy.

ENERGY

Sufficient energy must be provided to prevent endogenous protein catabolism, which results in malnutrition and exacerbation of azotemia. Although the energy requirements of dogs and cats that have chronic renal failure (CRF) are unknown, they are believed to be similar to those of healthy dogs and cats. Dogs should be fed $132 \times (\text{body weight in kilograms})^{0.75}$ per day and cats require 50 to 60 kcal/kg/d. Maintenance energy requirements may vary among individuals, and therefore energy intake should be customized based on serial determinations of body weight and body condition score. Carbohydrates and fats provide the nonprotein sources of energy in the diet. Typically diets designed for managing CRF are formulated with a high fat content because fat provides approximately twice the energy per gram than carbohydrate. This formulation results in an energy-dense diet that allows patients to obtain nutritional requirements from a smaller volume of food. A smaller volume of food minimizes gastric distention, which reduces the likelihood of nausea and vomiting.

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PROTEIN

Azotemia and uremia are caused by the accumulation of nitrogenous metabolites derived from excessive dietary protein or degradation of endogenous protein. High protein intake exacerbates azotemia and the morbidity of CRF [1], whereas protein malnutrition is strongly correlated with morbidity and mortality. The rationale for formulating a diet that contains a reduced quantity of high-quality protein and adequate nonprotein calories is based on the premise that controlled reduction of nonessential protein results in decreased production of nitrogenous wastes, with consequent amelioration or elimination of clinical signs even though renal function may remain essentially unchanged. Studies have shown that modifying dietary protein intake can reduce blood urea nitrogen (BUN) and provide clinical benefits to dogs and cats with CRF [1–6].

Whether protein restriction alters progression of renal failure in dogs and cats is less uncertain [5,7,8,9–12]. Brown and colleagues [13,14] reported that protein restriction did not alleviate glomerular hypertension, hypertrophy, hyperfiltration, or progression in dogs with induced renal failure. Adams and colleagues [15] reported that protein and energy restriction had no effect on renal lesions or function in cats with induced renal failure. Similarly, Finco and colleagues [16] reported that protein restriction had no effect on the development of renal lesions or on renal function in cats with induced renal disease.

The minimal dietary protein requirements for dogs or cats with CRF are not known but are believed to be similar to the minimal protein requirements of healthy pets. However, this degree of restriction is necessary only in animals with profound renal failure, and more liberal prescriptions can be fed to dogs with greater renal function. The dietary protein intake should be adjusted to minimize excesses in azotemia while simultaneously avoiding excessive restriction of dietary protein because of the risk for protein malnutrition. If evidence of protein malnutrition occurs (hypoalbuminemia, anemia, weight loss, or loss of body tissue mass), dietary protein should be gradually increased until these abnormalities are corrected.

MINERALS AND ELECTROLYTES

Phosphate retention and hyperphosphatemia occur early in renal disease and play a primary role in the genesis and progression of renal secondary hyperparathyroidism, renal osteodystrophy, relative or absolute deficiency of 1,25-dihydroxyvitamin D, and soft tissue calcification. By minimizing hyperphosphatemia, secondary hyperparathyroidism and its sequela can be prevented. In addition, dietary phosphorus restriction has been shown to slow the progression of renal failure in dogs and cats. In one study of dogs with surgically induced reduced renal function, those fed a low phosphorous diet (0.44% dry matter [DM]) had a 75% survival versus a 33% survival in those fed a high phosphorous diet (1.44% DM) [17]. Renal function also deteriorated more rapidly in the high phosphorous group. Ross and colleagues [18] reported that cats with reduced renal mass fed a phosphorus-restricted diet (0.24% DM) showed

little or no histologic change compared with those fed a normal phosphorus diet (1.56% DM), who showed mineralization, fibrosis, and mononuclear cell infiltration.

The goal of dietary therapy is to normalize the serum phosphate concentration, which may be achieved by limiting dietary phosphate intake. If normophosphatemia cannot been accomplished within 2 to 4 weeks of implementing dietary phosphate restriction, intestinal phosphate binders should be added to the treatment plan. Normalization of serum phosphate concentrations using these methods has been associated with a reduction in serum parathyroid hormone concentrations in cats with naturally occurring renal disease [19]. Parathyroid hormone concentrations may even return to the normal range [19].

Hypertension is common in dogs and cats with CRF [20–22], and has been implicated as a contributor to the progression of renal failure [21,22]. Jacob and colleagues [22] reported that dogs with naturally occurring chronic renal disease and systolic blood pressure higher than 180 mm Hg were more likely to develop a uremic crisis and die than dogs with normal systolic blood pressure. Furthermore, the risk for developing a uremic crisis and dying increased significantly as systolic blood pressure increased.

Sodium restriction has been recommended to alleviate hypertension associated with failure of the kidneys to excrete sodium. A report recently suggested that feeding more than 1.5 g of Na per 1000 kcal could promote progression of feline renal disease in its early stages [23]. However, altering sodium intake from 0.5 to 3.25 g Na per 1000 kcal did not influence development of hypertension or affect glomerular filtration rate in dogs with surgically induced renal reduction [24,25]. In addition, a recent study by Burankarl and colleagues [26] in cats with surgically induced moderate renal disease did not show any adverse effects associated with feeding 2 g Na per 1000 kcal [26]. These investigators also suggested that NaCl restriction (0.5 g Na per 1000 kcal) could activate neurohumoral axes that contribute to the progression of renal disease and exacerbate renal potassium wasting. A study of diet and lifestyle variables of cats with naturally occurring CRF suggested that increased dietary sodium intake was associated with decreased odds of developing CRF [27]. Therefore, the ideal dietary sodium concentrations for dogs and cats with CRF are not clearly defined. Current recommendations are for normal to mildly restricted sodium diets. As renal failure progresses, patients' ability to rapidly adjust sodium excretion in response to changes in intake becomes severely impaired. If sodium intake is rapidly reduced, dehydration and volume contraction may occur, with the potential to precipitate a renal crisis. Hence, a gradual change from the pet's previous diet to the salt-restricted diet is recommended.

Potassium deficiency has been identified in cats with CRF. This deficiency is caused by a combination of urinary potassium loss and decreased potassium intake [28]. However, not all cats are hypokalemic. One study reported that 13% of 116 cats with CRF were hyperkalemic, emphasizing the need to monitor potassium status and adjust intake with oral potassium gluconate on an individual basis [29].

ACID–BASE BALANCE

The kidneys excrete metabolically derived nonvolatile acid (sulfates, hydrogen ions) and are central to maintaining an acid–base balance. As renal function declines, the capacity to excrete hydrogen ions and reabsorb bicarbonate ions is reduced and metabolic acidosis ensues. Metabolic acidosis increases renal ammoniagenesis, which activates complement, contributing to the progression of renal failure. In addition, metabolic acidosis increases catabolism and degradation of skeletal muscle protein, disrupts intracellular metabolism, and promotes dissolution of bone mineral, exacerbating azotemia, loss of lean body mass, and renal osteodystrophy. Because dietary protein restriction results in the consumption of reduced quantities of protein-derived acid precursors, supplementation with additional alkalinizing agents, such as sodium bicarbonate, calcium carbonate, or potassium citrate, may be required.

LONG-CHAIN OMEGA-3 FATTY ACIDS

Long-chain omega-3 fatty acids compete with arachidonic acid and alter eicosanoid, thromboxane, and leukotriene production [30]. Remnant kidney studies in dogs have reported that omega-3 fatty acid supplementation (menhaden fish oil) reduces inflammation, lowers systemic arterial pressure, alters plasma lipid concentrations, and preserves renal function [31–34]. Because they cause an acute increase in glomerular filtration rate, omega-6 fatty acids (safflower oil) appear to be detrimental in dogs with naturally occurring renal disease [35]. Some commercially available diets have an adjusted omega-6:omega-3 ratio. However, focusing on the absolute concentrations of specific omega-3 fatty acids, rather than on ratios, would be more appropriate, but no studies have been reported. Studies of the effect of variation in dietary fatty acid composition in cats with renal disease have also not been reported.

FIBER

Fermentable fiber is a recent addition to the nutritional management of CRF. Experts hypothesize that fermentable fiber provides a source of carbohydrates for gastrointestinal bacteria, which consequently use blood urea as a source of nitrogen for growth. The increased bacterial cell mass increases fecal nitrogen excretion and has been suggested to decrease the BUN concentration and reduce the need for protein restriction. However, the major concern is that, unlike BUN, the molecular sizes of classical uremic toxins (middle-molecules) are too large to readily cross membrane barriers, and therefore the bacterial use of ammonia is unlikely to reduce these toxins. Furthermore, studies documenting these changes have not been reported. As a consequence, widespread application of fermentable fiber as a nitrogen trap currently cannot be recommended.

However, fermentable fibers have beneficial effects for modulating gastrointestinal health in patients who have CRF. New food supplements, including fiber-like polysaccharides derived from chitin and bacterial products, have recently been marketed as phosphate binders and agents that reduce azotemia, respectively. Although limited studies show a measurable reduction in

phosphate, BUN, and creatinine with supplementation, maximal effects occur in combination with nutritional therapy [36–38].

ANTIOXIDANTS

Endogenous oxidative damage to protein, lipids, and DNA is believed to play an important role in the progression of renal disease in humans [39,40]. Nutrients such as vitamin E, vitamin C, taurine, carotenoids, and flavonols are effective antioxidants that trap free radical species. Humans who have CRF have been shown to have lower concentrations of vitamin E and vitamin C and high concentrations of markers of lipid peroxidation [41]. These studies suggest that humans who have CRF experience oxidative stress. Studies in rats have suggested that supplementation with vitamin E may modulate tubulointerstitial injury and glomerulosclerosis, suggesting that vitamin E may slow progression of renal damage [42,43]. Although no studies have evaluated oxidative stress or antioxidant status in dogs or cats that have renal disease, ensuring adequate antioxidant intake seems prudent to minimize oxidative stress.

FEEDING STRATEGY

Dietary therapy is only effective in ameliorating the clinical signs of uremia if it is administered appropriately. Patients who have CRF are often anorexic and have reduced appetites. Practical measures to improve intake include the use of highly odorous foods, warming the foods before feeding, and stimulating eating by positive reinforcement with petting and stroking. Although appetite stimulants, such as the benzodiazepam derivatives or serotonin antagonists, may be judiciously administered, more aggressive therapy, such as esophagostomy or gastrotomy tube feeding, is clinically indicated in these cases. Instituting dietary changes when patients are hospitalized is inadvisable because these patients have a high risk for developing food aversion. The renal support diet should instead be instituted at home when the pet is stable and in a comfortable environment.

CLINICAL STUDIES OF NATURALLY OCCURRING CHRONIC RENAL FAILURE

Elliott and colleagues [4] evaluated the effect of a modified protein, low phosphate diet on the outcome of 50 cats with stable, naturally occurring CRF. Of these, 29 received a modified protein, low phosphate diet, and the remaining 21 received their normal diets. The two groups had no significant differences in age, body weight, creatinine, phosphate, and parathyroid hormone concentrations at the start of the study. The median survival time of the cats fed the modified protein, low phosphate diet was significantly greater than that of those fed the normal diet (633 days vs. 264 days, $P < .0036$). Of the cats on the normal diet, 69% died of progressive renal failure. The median survival time for cats fed a renal diet was 2.4 times longer than for cats fed a maintenance diet. These results suggest that feeding a renal diet to cats with CRF doubles their life expectancy.

Ross and colleagues [44] evaluated the effect of a renal diet (modified in protein, phosphorus, sodium, and lipids) compared with an adult maintenance diet in 45 cats that had stage 2 or 3 kidney disease. Of the 23 cats fed the adult maintenance diet, 6 experienced an uremic crisis, whereas none of the 22 cats fed the renal diet experienced an uremic crisis. At the end of the study, 5 of the 23 cats fed the adult maintenance diet died from renal-related causes. No renal-related deaths occurred in the 22 cats fed the renal diet. The results of this study suggest that dietary modifications can reduce the number of uremic crises and the mortality in cats that have naturally occurring stage 2 or 3 renal disease.

The effect of a modified protein, low phosphate diet on the outcome of dogs that have stable, naturally occurring CRF has also recently been shown [2]. Dogs with mild to moderate CRF fed a renal diet experienced a 70% reduction in the relative risk for developing a uremic crisis, remained free of uremic signs almost 2.5 times longer, and had a median survival that was three times longer than those with CRF fed a maintenance diet. Renal function declined more slowly in the dogs fed the renal diet. In dogs fed the maintenance diet, the primary cause of death was renal-related.

MONITORING

Regular monitoring to ensure that dietary and medical management remain optimal for the needs of the patient is crucial for the well-being and long-term successful treatment of patients who have CRF. Frequent patient evaluation may also improve owner compliance. Patients should be reevaluated within 2 weeks of initiating nutritional therapy and then three to four times per year. A complete dietary history, physical examination, body weight, body condition score, and laboratory evaluation are indicated. The dietary history should include the type of diet (dry vs. wet), the amount eaten each day (eaten is more important than amount offered), and the method of feeding, and should also note all treats, snacks, and supplements. This information is invaluable for monitoring the response to dietary therapy.

SUMMARY

CRF is the clinical syndrome resulting from irreversible loss of the metabolic, endocrine, and excretory capacities of the kidney. Nutrition has been the cornerstone of management for decades. The goals of dietary modification are to meet the patient's nutrient and energy requirements; alleviate clinical signs and consequences of uremia; minimize disturbances in fluid, electrolyte, vitamin, mineral, and acid–base balance; and slow progression of renal failure. Regular monitoring to ensure that dietary and medical management remain optimal for the needs of the patient is crucial for the well-being and long-term successful treatment of patients who have CRF.

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