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STAGED MANAGEMENT OF CHRONIC KIDNEY DISEASE IN DOGS AND CATS

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Optimum therapy of dogs and cats with CKD requires a thorough initial evaluation of the patient combined with adequate monitoring of both the natural course of CKD and the patient's response to intervention. Conservative medical management of CKD can be synthesized into the following four general treatment goals: 1) provide adequate and appropriate nutritional support, 2) correct deficits and excesses in fluids, acid-base and electrolytes (i.e. sustain a normal internal milieu), 3) ameliorate clinical signs of CKD, and 4) provide renoprotective therapy to slow progression of CKD. The following guidelines provided provide a framework for achieving these treatment goals.

Nutrition. Because hyporexia and anorexia and their associated adverse nutritional effects progressively lead to a devastating deterioration in the patient's quality of life, it is essential that they be recognized and responded to appropriately early in the course of CKD. The signpost that should be sought is whether the patient is meeting the nutritional goals of a stable body weight at an acceptable nutritional status (measured as a body condition score and assessment of activity and strength).

There is strong evidence supporting a recommendation to feed a renal diet to dogs and cats with serum creatinine concentrations in excess of 2.0 mg/dl (176 μ mol/l; CKD Stages 3 and 4 in dogs and mid-2 through 4 in cats). Benefits shown to accrue from dietary therapy in dogs and cats include preventing or delaying the onset of uremia and premature death due to complications of CKD. At least in dogs, these benefits have been shown to accrue, at least in part, from slowing progression of CKD. Importantly, in these diets have been shown to maintain or improve nutrition compared to consumption of a maintenance type diet. A common misconception is that renal diets are simply "low protein diets." Renal diets encompass a variety of modifications beyond just a limitation of protein content, and, indeed, the principal beneficial effects of these diets may not accrue from their protein content. Thus, simply replacing a renal diet with a standard manufactured diet that is lower in protein content does not meet the guideline of feeding a renal diet. Since inappropriate diets can exacerbate clinical signs of uremia and/or promote progression of CKD, cats and dogs with CKD should be fed a renal diet.

Owners often consider food consumption to be a premier indicator of their pet's quality of life, and they are often happy when their pet shows any interest in food. However, it is inappropriate to accept the pet's consumption of "some" food as a goal of therapy. Malnutrition is a major cause for morbidity and mortality in dogs and cats with CKD stages 3 and 4. Ideally patients should consume sufficient calories from an appropriate diet to maintain a body condition score of 4 to 5/9. Increased efforts are indicated to assure sufficient calorie intake for patients with body condition scores of 3/9 or lower or when patients fail to consume adequate calories to maintain a stable, appropriate body weight. In addition to inattention to adequate nutrition, some factors that may contribute to malnutrition in dogs and cats with CKD include consumption of inappropriate diets and metabolic factors related to uremia (especially uremic gastrointestinal signs and metabolic acidosis). Failure to adequately address uremic gastritis, uremic stomatitis and dental health can promote anorexia. Metabolic acidosis can promote protein catabolism and malnutrition.

It is appropriate to consider placing a feeding tube when patients fail to spontaneously consume adequate food. Feeding via gastrostomy or esophagostomy tube is a simple and effective way to provide an adequate intake of calories and water. In addition, feeding tubes simplify drug administration. Based on this line of reasoning, use of feeding tubes has been recommended for CKD patients.

Deficits and excesses in fluids, acid-base and electrolytes. Excessive phosphorus intake and inappropriately high serum phosphorus concentrations appear to promote progressive kidney injury. Intervention to manage serum phosphorus concentration is indicated for dogs and cats with CKD stages 2-4 when serum phosphorus concentration rises above stage-specific therapeutic target concentrations. Ideally, serum phosphorus concentration should be maintained below 4.5 mg/dl (1.4 mmol/L) in stage 2, below 5.0 mg/dl (1.6 mmol/L) in stage 3 and below 6.0 mg/dl (1.9 mmol/L) in stage 4 CKD. When serum phosphorus concentration exceeds these target concentrations, dietary phosphorus restriction should be initiated using a renal diet. In most dogs and cats with CKD stages 2 and 3, dietary phosphorus restriction alone will maintain the desired serum phosphorus concentration below the target concentration. However, in some CKD stage 3 patients and most CKD stage 4 patients, addition of an intestinal phosphate binding agent will be necessary to reduce serum phosphorus concentration below the target concentration.

The most commonly used intestinal phosphate binding agents in dogs and cats contain aluminum as hydroxide, oxide or carbonate salts. Aluminum-containing binding agents generally appear to be well tolerated and safe in dogs and cats; as such, they probably represent first choice drugs for phosphate binding. Alternative drugs that do not contain aluminum include calcium carbonate, calcium acetate, sevelamer hydrochloride, or lanthanum carbonate. Experience with these drugs in dogs and cats are limited, but hypercalcemia may be a problem with the calcium-based products, particularly when administered with calcitriol. An intestinal phosphate binder composed of a mixture of calcium carbonate and chitosan is currently marketed for use in dogs and cats.

Intervention to correct metabolic acidosis is indicated for dogs and cats with CKD stages 1-4 when blood bicarbonate concentration drops below the therapeutic target range of 18 to 24 mmol/L. Metabolic acidosis in CKD results primarily from impaired renal ammoniagenesis, although impaired excretion of titratable acid and impaired reabsorption of bicarbonate may contribute as well. Clinical effects of metabolic acidosis may include progressive renal injury and increased protein catabolism with loss of lean tissue. Treatment of metabolic acidosis involves administration of an alkalinizing salt, usually sodium bicarbonate or potassium citrate, in sufficient amount to increase blood bicarbonate concentration into the normal range.

Intervention to correct and prevent dehydration is indicated for dogs and cats with CKD stages 2-4 with clinical evidence of dehydration. Maintenance of hydration in CKD depends on adequate compensatory polydipsia. Cats with CKD appear to be particularly susceptible to chronic dehydration, perhaps because the magnitude of compensatory polydipsia is inadequate. However, lack of adequate access to good quality drinking water, certain environmental conditions and intercurrent illnesses that limit fluid intake or promote fluid losses (e.g. pyrexia, vomiting or diarrhea) may lead to dehydration. The clinical consequences of chronic dehydration include decreased appetite, lethargy, weakness, constipation, prerenal azotemia, and predisposition to acute kidney injury. Additional loss of kidney function due to acute kidney injury is a potentially important cause for progression of CKD. The goal of therapy is to correct and prevent dehydration and its clinical effects.

In patients with signs consistent with chronic or recurrent dehydration, long-term subcutaneous fluid therapy may be considered. Typically, a balanced electrolyte solution (e.g. lactated Ringer's solution) is administered subcutaneously every one to three days as needed. The volume administered depends upon patient size with a typical cat receiving about 75 to 100 ml per dose. If the clinical response of the patient is suboptimal, the dose can cautiously be increased. However, it is possible to induce fluid overload with excessive administration of fluids. In addition, sodium-containing fluids used for subcutaneous therapy do not provide electrolyte-free water. A more physiologically appropriate approach is to provide water via a feeding tube. This approach may also be easier for clients. Because recent evidence suggests excessive sodium intake may harm the kidneys, recommendations for long-term sodium administration in any form should be carefully considered.

Ameliorate clinical signs of uremia. Treatment of anemia of CKD is indicated in CKD stages 3 and 4 when the hematocrit declines below 22 % and the patient has clinical signs attributable to anemia.

The goal of treatment is increasing the hematocrit to approximately 30 to 40% in cats and 38 to 48% in dogs. Signs attributable to anemia may include impaired appetite, lethargy, weakness, and decreased social interaction. Administration of erythropoietin, either as recombinant human erythropoietin (rHuEPO; Epogen®, Procrit®) or darbepoietin (Aranesp®) is the only effective means of correcting anemia of CKD. However, other factors that may exacerbate anemia, including blood loss, iron deficiency, poor nutrition, hyperparathyroidism, and infections, should be ruled-out first. Anti-erythropoietin antibodies may develop in some rendering them unresponsive to further rHuEPO treatment. Therapy should be terminated immediately if antibody-associated anemia is suspected. Since canine and feline species-specific EPO is not available, patients treated with rHuEPO should be monitored closely for recurrence of anemia which may herald the onset of anti-EPO antibodies. A newer, longer-acting erythropoietin, Darbepoietin, may be less likely to induce anti-erythropoietin antibodies; however, experience with darbepoietin in dogs and cats is limited.

Dogs and cats in CKD Stages 3 and 4 may have gastrointestinal complications of CKD including reduced appetite with reduce food intake, nausea, vomiting, uremic stomatitis and halitosis, gastrointestinal hemorrhage, diarrhea, and hemorrhagic colitis. Treatment for these gastrointestinal signs largely focuses on ameliorating "uremic gastritis" by: 1) limiting gastric acidity using H₂ blockers (ranitidine, famotidine), 2) suppressing nausea and vomiting using antiemetics (metoclopramide, 5-HT₃ receptor antagonists such as ondansetron HCl or dolasetron mesylate), or low doses of phenothiazine tranquilizers (prochlorperazine), and 3) providing mucosal protection using sucralfate. Of these treatments, H₂ blockers are most commonly employed and few adverse effects have been attributed to their use. Antiemetics are typically added when anorexia, nausea or vomiting persist despite the use of an H₂ blocker. Sucralfate is added when gastrointestinal ulcerations and hemorrhage are suspected.

Provide renoprotective therapy to slow progression of CKD. Glomerular proteinuria should be reduced in dogs and cats with CKD stages 1 through 4. Intervention is indicated when the urine protein-to-creatinine ratio (UPC) exceeds 2.0 in dogs and cats with CKD stage 1, and when the UPC exceeds 0.5 in dogs and 0.4 in cats with CKD stages 2 through 4. Proteinuria has been shown to adversely affect outcomes in humans, dogs and cats with CKD, presumably because proteinuria itself appears to injure the renal tubules, thereby promoting progression of CKD. It is well established in human patients that reducing proteinuria by suppressing the renin-angiotensin-aldosterone system ameliorates the adverse effects of proteinuria on the kidneys. Although qualitatively similar, evidence in dogs and cats is far less compelling. Nonetheless, an ACE inhibitor (e.g. enalapril, benazepril, lisinopril) is recommended for CKD patients that meet the above criteria. Ideally, proteinuria should be reduced below the therapeutic target.

Drug therapy to lower blood pressure is indicated in dogs and cats with CKD stage 2 through 4 when blood pressure exceeds 160/100 mmHg and dogs and cats with CKD stage 1 when blood pressure exceeds 180/120. Unless evidence of hypertensive retinal lesions or central nervous system lesions are present, blood pressure values should be determined on at least 3 separate episodes before establishing the need for therapeutic intervention. The goal of therapy is to reduce blood pressure below 160/100 mmHg.

Amlodipine is the first-choice drug for managing elevated blood pressure in cats with CKD (evidence grade 2). It is typically highly effective in reducing blood pressure in cats, often by as much as 20 to 50 mmHg. Hypertension in dogs appears to be more resistant to drug therapy. Because ACE inhibitors reduce intraglomerular pressure even when systemic blood pressure is not effectively ameliorated, these drugs have a therapeutic advantage as first line drugs in dogs with CKD in mitigating the renal effects of hypertension. However, since ACE inhibitors are often relatively ineffective antihypertensive drugs in dogs, amlodipine is typically combined with ACE inhibitor therapy to achieve the therapeutic goal.

Calcitriol is indicated for dogs with CKD stages 3&4 to slow progression of CKD and extend survival (evidence grade 1). However, calcitriol therapy should not begin until the patient's serum phosphorus concentration is 6.0 mg/dl or less. Evidence supporting calcitriol therapy in cats is weak.