

Chronic kidney disease in dogs and cats II: Principles of management



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Chronic kidney disease cannot be cured, but it can be treated effectively. As Jill Maddison and Harriet Syme explain, clinical signs may be ameliorated and progression of disease attenuated by a combination of therapeutic interventions

Fluid therapy is an essential component of the management of Chronic kidney disease (CKD) as hypovolaemia and hypotension caused by inadequate fluid therapy will exacerbate renal damage. Although CKD cannot

be cured, patients can often receive substantial benefit from intravenous fluid therapy to restore hydration and increase excretion of nitrogenous waste products prior to initiation of palliative therapy such as low protein diets. It

should be noted that patients with CKD are unable to dilute as well as concentrate urine, and therefore, are susceptible to overhydration as a result of overzealous fluid therapy. Correction of dehydration and underlying precipitating factors as well as a few days of adequate diuresis, will often vastly improve patients' clinical status and allow them a further, often extended, period of relatively good health. It is, however, unusual for this optimistic scenario to apply to patients with very high urea and creatinine concentrations. It should be realised that reducing the 'numbers' is a fairly futile exercise if the patient rapidly re-equilibrates to its previous degree of azotaemia after leaving the hospital. The fluid rate should be approximately twice normal maintenance rates. Maintenance rates equal approximately 50 mL/kg/day (more for small animals, less for larger animals) thus an approximate rate of 100 mL/kg/day is usually appropriate. This may need adjustment in individual patients. Dehydration should be corrected (5% dehydration = 50 mL/kg fluids) over 12 to 24 hours unless that patient has concurrent cardiac disease in which case fluid replacement should be slower. If the patient is hypovolemic, then an initial fluid bolus may be beneficial.

Selection of fluids

In patients with CKD, short term use of a balanced electrolyte solution is usually adequate. More prolonged fluid therapy requires both 5 per cent dextrose in water, as well as a balanced electrolyte solution with added potassium chloride. Cats may require more potassium supplementation than dogs.

MANAGEMENT OF ACID/BASE AND ELECTROLYTE IMBALANCES

Metabolic acidosis

Metabolic acidosis commonly develops in patients with severe CKD. However, in many instances in CKD, acidemia occurs when there is concurrent dehydration and rehydration will resolve the acidemia without specific alkali therapy being required. Some animals with CKD may benefit from oral therapy with sodium bicarbonate (8-12 mg/kg bid-tid). However, blood gas analysis is required to monitor the need for, and response to, therapy. Renal care diets are typically formulated to be slightly alkalinising to address this concern.

Hyperphosphataemia

Hyperphosphataemia should be minimised in patients with CKD as it plays a central role in the genesis and progression of renal secondary hyperparathyroidism and renal osteodystrophy and may promote progression of chronic renal failure.

The first line of management is to restrict dietary phosphate intake. As meat and dairy products are important sources of dietary phosphate, dietary protein restriction results in reduced phosphate intake. If dietary restriction alone fails to prevent hyperphosphataemia, phosphate binding agents may be administered. Aluminium-containing antacids are usually

used for this purpose (30-90 mg/kg/day). Recently lanthanum carbonate (Renalzin) has been marketed as a 'nutraceutical' for treatment of renal failure. It is not absorbed from the intestine and seems to be safe and effective if given in sufficient doses. The potential advantage of this drug is that it is available as a tasteless liquid and is applied via a pump dispenser so it may be better accepted by patients than other phosphate binders. Like aluminium hydroxide it may predispose patients to constipation. Calcium carbonate has also been recommended but has the disadvantage of potentially causing hypercalcaemia. The significant phosphate binding effects of Ipakitine are provided by the calcium carbonate it contains but the product does have a fishy smell which may be appealing to patients.

LOW PROTEIN DIETS

The rationale for restricting protein intake of patients with CKD is based on the premise that controlled reduction of non-essential proteins will result in decreased production of nitrogenous wastes. However, studies have shown that excessive restriction of protein is just as detrimental as high protein diets in dogs. Therefore, only moderate protein restriction is usually required. One of the most important and practical reasons to restrict protein in dogs with renal disease is that it is very difficult to achieve the restriction of phosphate that is required without also restricting protein. Although a direct cause and effect relationship has not been proved, it is believed that retained protein catabolites may contribute significantly to the clinical syndrome of uraemia.

There is no evidence to suggest that the feeding of low protein diets to patients with asymptomatic azotaemia (i.e., impaired urine concentration and mild to moderate azotaemia but no clinical signs such as inappetence or vomiting) is beneficial. The theory that protein restriction prevents self-perpetuating renal damage was based on studies in rats. However, these diets may prove beneficial because of the phosphate restriction that results from feeding a low protein diet. Protein restriction has not been demonstrated to be beneficial in dogs with experimentally-induced renal failure. There are no studies in dogs with naturally occurring renal failure that document that protein restriction slows the progression of renal damage. One justification for feeding such diets to asymptomatic patients might be to enable them to become accustomed to a different diet before they develop a more finicky and perhaps reduced appetite.

SODIUM BALANCE

Animals with chronic renal failure have limited capacity to adapt to wide fluctuations in sodium intake. In the past, it had been recommended that animals with chronic renal failure be fed diets high in sodium (to promote diuresis), but it is now recommended that they be fed normal (as opposed to restricted or high) sodium diets. Sodium restriction does not appear to alter blood pressure in cats, but may cause activation of the renin-angiotensin system, so it is also not recommended.

NON-REGENERATIVE ANAEMIA

Anaemia in chronic renal failure is often mild and has little clinical impact. However, moderate to severe anaemia may have significant clinical effects. Androgen therapy is reported to be useful in humans with end stage renal disease, but the efficacy of androgens in dogs and cats with renal failure has not been critically evaluated.

Androgens stimulate erythropoiesis by direct effects on pluripotential stem cells and erythroid progenitor cells and by stimulating erythropoietin production. Response to these drugs is likely to be slow and minor.

Blood transfusion is occasionally indicated for patients who have severe anaemia and clinical signs referable to their anaemia. However, transfusions will only be transiently effective.

Recombinant human erythropoietin (rHu-EPO) has been used to treat the non-regenerative anaemia that occurs in chronic renal failure. Treatment is usually limited to patients with sufficiently severe anaemia to be causing clinical signs.

The therapeutic goal of rHu-EPO therapy is a PCV in the low-normal range. Overzealous treatment can result in hypertension and seizures. In approximately 30 per cent of patients, EPO treatment will become ineffective due to the development of antibodies against the drug. Unfortunately these antibodies cross-react with endogenous

erythropoietin resulting in anaemia that can only be treated by blood transfusion. Recently, a longer acting formulation of rHu-EPO (darbepoetin) has been developed and anecdotally this may be associated with a lower incidence of antibody development. This is dosed at 6.25 µg/cat or 6.25 µg/8 kg in the dog and is given once weekly initially. This may be reduced to even less every fortnight once the PCV starts to climb. It must be noticed that this drug is expensive.

URINARY TRACT INFECTION

Urinary tract infections are common in patients with chronic renal failure. Because urinary tract infection is often detected at the time the patient presents with overt signs of renal failure, it is often erroneously assumed that infection is the primary cause of the renal disease. Although pyelonephritis can cause renal failure, it is important to recognise that many urinary tract infections in dogs and cats with CKD are secondary.

Although it is important to treat infection to prevent septicaemia and further exacerbation of renal function, resolution of infection will usually not resolve the underlying renal disease although in some cases this does result in quite marked clinical improvement in the patient. Antimicrobial therapy should be selected with care and the route of drug excretion and potential for nephrotoxicity considered.



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ACE INHIBITORS

There is evidence that use of ACE inhibitors (such as benazapril) will attenuate the progression of renal failure in humans and animals with significant proteinuria. However, the evidence that they are beneficial in patients with mild proteinuria (the majority of cats) has not yet been clearly established. There is a rationale for using ACE inhibitors in cats and dogs with renal failure as there may be some benefit provided the patient can be pillled easily and the owner can afford the treatment. However, dietary change (reduction in phosphate) carries significantly greater potential benefits in slowing the progression of non-proteinuric renal failure and ACE inhibitor therapy should not be regarded as a substitute for it. Treating cats and dogs that are severely azotaemic, or that have pre-renal azotaemia with ACE-inhibitors may actually speed their demise.

ANTI-HYPERTENSIVE AGENTS

Amlodipine (Istin, a calcium channel blocker) is the currently recommended treatment for hypertension in cats. This is because other treatments (β -blockers, ACE-inhibitors) do not reduce the blood pressure sufficiently to prevent the development of ocular lesions. The initial dose of amlodipine is 0.625 mg (1/8 tablet) per cat, per day. If this dose does not reduce the blood pressure sufficiently (i.e. to <165 mm Hg), then the dose is doubled to 1.25 mg (1/4 tablet). This dose is adequate in almost all cats. Where a poor response is noted, it is generally due to poor owner or cat compliance. Hypertension in dogs with CKD is poorly responsive to treatment. Treatment with an ACE-inhibitor (eg. enalapril 0.5 mg/kg day), is generally considered to be the first line of treatment, especially if the dog is proteinuric, and if this does not reduce the SBP then a conservative dose of amlodipine (0.05-0.2 mg/kg day) may be used in addition to this.

CHRONIC KIDNEY DISEASE IN DOGS AND CATS II: PRINCIPLES OF MANAGEMENT OF THE STATEMENTS BELOW, WHICH ARE TRUE AND WHICH ARE FALSE?

1. It is important to monitor fluid rates carefully in patients with CKD.
2. A balanced electrolyte solution such as Hartmanns is an appropriate fluid choice for most patients with CKD.
3. Reduction of hyperphosphataemia is one of the most important aims of in managing a patient with CKD.
4. It is important to restrict protein as much as possible in a patient with CKD
5. If a patient has mild azotaemia due to CKD but is asymptomatic it is beneficial to restrict protein in their diet.
6. The most important treatment for patients with CKD is use of ACE inhibitors.

ANSWERS

1. True: Hypovolaemia and hypotension caused by inadequate fluid therapy will exacerbate renal damage. Patients with CKD are unable to dilute as well as concentrate urine and therefore are susceptible to overhydration as a result of overzealous fluid therapy. Twice maintenance fluid rates are usually appropriate (but patient must be monitored) once dehydration has been corrected.
2. False: In patients with CKD, short term use of a balanced electrolyte solution is usually adequate; however, more prolonged fluid therapy requires both 5% dextrose in water as well as a balanced electrolyte solution with added potassium chloride. Cats may require more potassium supplementation than dogs.
3. True: Hyperphosphataemia should be minimised in patients with CKD as it plays a central role in the genesis and progression of renal secondary hyperparathyroidism and renal osteodystrophy and may promote progression of chronic renal failure.
4. False: While one of the most important and practical reasons to restrict protein in dogs with renal disease is that it is very difficult to achieve the restriction of phosphate that is required without also restricting protein. However, studies have shown that excessive restriction of protein is just as detrimental as high protein diets in dogs. Therefore only moderate protein restriction is usually required.
5. False: There is no evidence to suggest that the feeding of low protein diets to patients with asymptomatic azotaemia (i.e. impaired urine concentration and mild to moderate azotaemia but no clinical signs such as inappetence or vomiting) is beneficial.
6. False: There is evidence that use of ACE inhibitors (such as benazapril) will attenuate the progression of renal failure in humans and animals with significant proteinuria. However, the evidence that they are beneficial in patients with mild proteinuria (the majority of cats) has not yet been clearly established. There is a rationale for using ACE inhibitors in cats and dogs with renal failure as there may be some benefit provided the patient can be pillled easily and the owner can afford the treatment. However, dietary change (reduction in phosphate) carries significantly greater potential benefits in slowing the progression of non-proteinuric renal failure and ACE inhibitor therapy should not be regarded as a substitute for it.