ACUTE KIDNEY INJURY IN CATS: PART THREE – MANAGEMENT

Author : NATALIE FINCH

Categories : [Vets](#)

Date : January 12, 2015

NATALIE FINCH BCSc, Phd, MRCVS considers management techniques for AKI, including fluid therapy, and how to deal with the potential complications that may arise during treatment

PART one of this article (VT44.48) discussed the pathophysiological process, varying aetiologies and prognosis of acute kidney injury (AKI) in cats and part two (VT44.49) discussed the diagnosis. Part three's focus will be its management.

Management of AKI

The management goal in acute kidney injury (AKI) is, firstly, to prevent further renal damage by identifying and treating any primary underlying cause appropriately and, secondly, to enhance renal cellular recovery.

Potential treatable underlying diseases include pyelonephritis, urinary tract obstruction or lymphoma. If the cat has a very recent history of toxin ingestion, then inducing emesis or the administration of activated charcoal as an absorbent may be beneficial. The Veterinary Poisons Information Service provides up-to-date information regarding management and is contactable 24 hours a day (www.vpisuk.co.uk or 020 7188 0200). The key management strategies for AKI patients include maintaining renal perfusion and oxygen delivery, maintaining urine output and addressing secondary complications of AKI.

Fluid therapy

Fluid volume status should be addressed first. AKI patients can range from dehydrated or hypovolaemic to fluid volume overloaded. Dehydrated or hypovolaemic patients should receive appropriate fluid administration to correct any deficit and become volume replete. Dehydration or hypovolaemia can result in reduced renal blood flow (RBF) and consequently decreased glomerular filtration rate (GFR) and urine formation, and contribute to further renal injury. In patients with pre-renal AKI, the changes are potentially reversible if the haemodynamic abnormalities are identified and corrected quickly. Care must be taken with fluid administration as overzealous fluid administration can result in fluid volume overload, particularly in oliguric or anuric patients. In human patients, studies have shown increased mortality rates in patients with liberal fluid administration compared to those with more restrictive plans[1]. Drip pumps and syringe drivers are invaluable for delivering accurate fluid volumes to cats. Fluid therapy is also important (Figure 1) in correcting electrolyte imbalance and acid-base disorders.

Compound sodium lactate (Hartmann's solution, lactated Ringer's) would be an appropriate fluid to administer in most cases. Physiologic saline (0.9 per cent NaCl) may be more suitable for patients with hypochloraemia, hyponatraemia or severe secondary hyperkalaemia. Fluid resuscitation in hypovolaemic or hypotensive cats should involve a fluid bolus of 10ml/ kg to 15ml/kg administered over 10 minutes to 20 minutes. The cat should be reassessed and boluses repeated until the patient becomes haemodynamically stable. Ongoing fluid rates should take into account fluid losses, such as urine output, vomiting or diarrhoea. In anuric patients, fluid rates should be carefully considered and it is recommended to replace insensible losses (respiration and faeces) only, which are approximately 22ml/kg/day.

Compromised renal tubules are unable to respond to any initial increase in GFR and tubular cell damage can also lead to solute loss. Therefore, there is an initial period of polyuria and solute diuresis in the early recovery stages of AKI. This can be challenging for clinicians to manage as large volumes of IV fluids are required and there may be significant electrolyte losses resulting particularly in hypokalaemia.

Once the patient becomes stable and the azotaemia has either resolved or stabilised, fluid therapy can be gradually tapered ensuring there is a corresponding decrease in urine output and no increase in creatinine concentration.

Urine output

Urine output should be monitored as accurately as possible, particularly in response to fluid therapy. This should ideally be achieved by placement of a urinary catheter and a closed collection system. Urinary catheter placement without a collection system should be avoided due to the risk of development of urinary tract infection. There is also a risk of iatrogenic urinary tract infection associated with catheter placement, and management of the catheter should be performed as aseptically as possible. If placement of a urinary catheter is not possible, then collecting and weighing naturally voided urine can provide some estimate (1g = 1ml). Normal urine output in a

healthy animal not on fluid therapy would be 1ml/kg/hr to 2ml/ kg/hr. Oliguria is defined as urine production less than 1ml/kg/hr and anuria as zero urine production. Once normal urine output is achieved and further monitoring is not required, the urinary catheter should be removed as its presence will increase the risk of urinary tract infection.

Urinary tract obstruction

If a urinary tract obstruction or rupture is identified, then placement of a urinary catheter or surgical intervention may need to be considered. Ureteral obstructions can be managed with placement of ureteral stents, although there are limited centres offering this.

Electrolytes

Hyperkalaemia is perhaps the most common secondary complication of AKI and results from decreased renal excretion of the cation. Severe hyperkalaemia (more than 6mmol/L) can result in cardiac arrhythmias, most commonly recognised as bradyarrhythmias. ECG monitoring is helpful for detection of arrhythmias. Typical ECG changes include prolonged QT interval, widened QRS complex and small or absent P waves. Hyperkalaemia can also be exacerbated by iatrogenic potassium administration or by certain drugs (beta-blockers, ACE inhibitors, spironolactone). Severe life-threatening hyperkalaemia can be managed with calcium gluconate, dextrose and/or insulin, sodium bicarbonate and, in rare cases, with beta agonists. Calcium gluconate will not decrease the potassium concentration, but will alter the membrane potential of cardiac myocytes, therefore offering cardioprotection. Administration of intravenous dextrose will stimulate insulin release, which will drive potassium intracellularly, although this effect is minor. Administration of exogenous insulin is more potent than stimulating endogenous insulin release, but is associated with the risk of hypoglycaemia and, therefore, should be administered in combination with dextrose.

Acid-base status

Metabolic acidosis is frequently recognised in AKI patients due to reduced bicarbonate production in the kidneys, reduced ability to excrete hydrogen ions and an increased concentration of uraemic acids. Consequences of metabolic acidosis include disruption of cellular metabolism, exacerbation of hyperkalaemia due to extracellular shift of potassium, with intracellular shift of hydrogen ions and increased protein and bone turnover.

Management of metabolic acidosis should focus on correcting fluid abnormalities and hypoperfusion, which may be contributing to lactic acidosis. Sodium bicarbonate should only be reserved for severe acidosis (pH

The dose of bicarbonate is calculated using the formula 0.3 × bodyweight (kg) ×(target bicarbonate concentration – actual bicarbonate concentration). It can be administered as a constant rate infusion over several hours.

Antibiotics

If there is an active sediment on urinalysis or suspicion of pyelonephritis then it may be prudent to start broad-spectrum antibiotics pending culture and sensitivity.

Hypertension

Many cats with AKI develop hypertension, with a recent study reporting 38 per cent of cats to have a systolic blood pressure greater than 150mmHg[2]. Clinical signs associated with this can include retinal detachment, hypertensive encephalopathy and seizures and progressive renal injury. Systolic blood pressure should be measured using the Doppler technique. The author considers a systolic blood pressure which is persistently greater than 160mmHg in a calm, non-fractious cat or greater than 160mmHg in combination with evidence of hypertensive retinopathy on fundic examination, as hypertensive. This would be moderate or high risk of target end organ damage, according to the American College of Veterinary Internal Medicine (ACVIM) hypertension consensus statement[3]. If hypertension is documented, then anti-hypertensive medication should be instigated. The calcium channel blocker amlodipine (0.625mg/cat to 1.25mg/cat PO SID) is the first-line drug of choice. If amlodipine is unsuccessful at decreasing blood pressure, then hydralazine may be considered (2.5mg/cat PO or SQ SID). ACE inhibitors should be avoided due to their ability to cause afferent arteriolar constriction and further reduce RBF. Conversely, hypotension (systolic blood pressure less than 80mmHg) should also be avoided to prevent further renal hypoperfusion and damage.

Anaemia

Anaemia is a further potential complication of AKI. This can develop due to gastrointestinal haemorrhage, inflammation, decreased red blood cell life span, hypocoagulability and tendency for haemorrhage due to thrombocytopathias, iatrogenic blood sampling, aggressive fluid therapy and reduced erythropoietin production. Gastroprotection can help reduce any gastrointestinal haemorrhage. Blood transfusions may ultimately need to be considered.

Gastrointestinal signs

Gastrointestinal signs and, in particular, vomiting is common in AKI patients. Vomiting may result from the direct effects of uraemic toxins on the chemoreceptor trigger zone causing a central nausea, uraemic gastritis/ulceration, delayed gastric emptying/ileus, reduced renal clearance of gastrin, leading to increased hydrochloric acid secretion or gastrointestinal oedema. Management should include administration of antiemetics, such as maropitant, metoclopramide or ondansetron, and antacids such as H_2 receptor antagonists (for example, famotidine) and proton pump inhibitors (for example, omeprazole).

Nutrition

Nutritional support should be considered in cats with AKI as they are generally anorexic and in a catabolic state. The placement of a feeding tube may be required. A naso-oesophageal feeding tube may be most appropriate as it can be placed with ease in a conscious patient, negating the need for general anaesthesia. Parenteral nutrition may be considered in some cases, but is less preferable. Placement of a feeding tube can also facilitate administration of medications and fluids. Ideally, a renal diet, which is both protein and phosphate restricted, should be fed. Oral phosphate binders can also be used in hyperphosphataemic patients.

Other treatments

Diuretic therapy

If a patient remains oligoanuric despite fluid therapy, then conversion to a non-oliguric state can be attempted with the use of diuretics. The use of diuretics is no longer recommended in human practice where dialysis is readily available. There are also risks of worsening kidney injury, or cardiovascular side effects associated with some agents. The use of diuretics should not be applied indiscriminately and careful risk-benefit assessment should be made before their use.

Furosemide would be the primary drug of choice to promote diuresis. It is important to remember the site of action of furosemide is the thick ascending loop of Henle and, therefore, if GFR is absent, furosemide will not reach the site of action to elicit an effect. Furosemide induces diuresis and natriuresis, but the increased urine flow does not have any effect on increasing GFR. Furosemide inhibits the sodium-potassium-chloride pump in the luminal cell membrane of the loop of Henle, which decreases transcellular sodium transport. Basal NaK-ATPase activity is, therefore, no longer necessary, which may reduce medullary oxygen requirement and protect against further renal injury. An increase in urine output should be seen between 20 and 60 minutes after IV administration of furosemide although, as discussed above, furosemide may not be effective. The diuretic effects of furosemide may also be beneficial in some patients in preventing fluid volume overload. Clinical studies evaluating the use of furosemide in cats with AKI are lacking. Furosemide, dopamine and fluid therapy in combination was found to increase urine output more significantly in healthy, awake cats compared to fluid therapy and mannitol, but did not alter GFR[4].

Mannitol is an osmotic diuretic and increases plasma osmolality. It therefore increases intravascular volume and promotes tubular fluid flow. It is also considered to act as a renal vasodilator to improve RBF and GFR and scavenges oxygen free radicals. Mannitol may also help to prevent further renal cell injury by preventing influx of calcium into mitochondria. Mannitol also causes natriuresis, possibly by stimulating atrial natriuretic peptide (ANP) production and inhibiting sodium and water reabsorption in the collecting ducts. The use of mannitol in cats with AKI has not been evaluated. Mannitol administration in combination with fluid therapy in healthy, awake cats did not have any significant effect on GFR and urine output compared to fluid therapy alone[4]. Mannitol should only be used when diuresis has been demonstrated (and should not be used in anuric cats). This is due to the risk of fluid volume overload. In addition, mannitol can exacerbate hyperkalaemia

via solvent drag of potassium with body water from the intracellular to extracellular space. Mannitol is not recommended in human AKI patients.

Dopamine, although once used historically, is not recommended. Dopamine acts on dopamine-1 (DA-1) and dopamine-2 (DA-2) receptors on renal arteries, causing pre-glomerular vasodilation and resulting in increased RBF and, subsequently, GFR. Possible side effects include hypertension and cardiac arrhythmias. Cats have lower numbers of dopamine receptors in the kidneys compared to dogs and humans[5] and are therefore considered to have reduced response to dopamine.

Fenoldopam is a selective DA-1 receptor agonist causing peripheral arterial vasodilation, increased RBF and GFR and diuresis. As fenoldopam is more specific to DA-1 receptors than dopamine, it may be associated with fewer side effects. In humans, its use is being studied in patients at risk of AKI and in patients with oliguric or anuric AKI. There is no data regarding its use in AKI in cats and dogs. In healthy dogs, which were exsanguinated to represent a model of hypovolaemia, it was demonstrated RBF, GFR and natriuresis were maintained, but not increased, suggesting, renoprotection in the face of acute ischaemic injury[6]. In cats, given the lower numbers of DA-1 receptors in the kidneys, the response is likely to be reduced; however, there is no clinical data to evaluate its use.

Renal replacement therapy

Renal replacement therapy (RRT) encompasses different forms of dialysis, which can be used to manage patients in renal failure (Figure 2). It is generally indicated only for those patients expected to regain renal function.

The principle is fluid and solutes can be transported across a semipermeable membrane and urea, creatinine, potassium, calcium and phosphate can move down a solute gradient into the dialysate. There are various dialysis modalities. Extracorporeal therapies take blood outside the body for purification and include intermittent renal haemodialysis and continuous renal replacement therapy, whereas peritoneal dialysis purifies blood within the body. Haemodialysis may also be helpful in removing excessive body water in patients that have become fluid volume overloaded and in correcting acidaemia. Evaluation of the potential use for removing toxins from the blood is also under way. Haemodialysis is not readily available in the UK as it requires extensively trained personnel to operate the facility. The RVC is the only centre to offer continuous RRT and further information can be found online (http://bit.ly/1s9fzXA). Peritoneal dialysis is labour intensive and associated with many complications. Peritoneal dialysis involves placement of a peritoneal catheter through which there is infusion of dialysate, which is allowed to remain in the peritoneal cavity for a set period of time before being removed.

Monitoring

Accurate monitoring of urine output in the AKI patient is important and should form a key part of

management. Monitoring hydration status is also essential. Not only can there be ongoing fluid losses as the result of vomiting, but marked polyuria can develop in the recovery phase, which can lead to dehydration. AKI patients are at high risk of becoming fluid volume overloaded. Monitoring of hydration status should include assessment of skin turgor, bodyweight, respiratory rate and lung auscultation, PCV/total solids, urinary output and blood pressure. Electrolytes, renal markers and blood pressure should be monitored regularly and, if possible, acid-base balance.

Pulmonary compromise can occur in AKI patients. Contributory factors include fluid volume overload, aspiration pneumonia and uraemic pneumonitis. Monitoring of respiration rate and regular thoracic auscultation may be helpful in detecting development of pulmonary compromise. Oxygen saturation status (using a pulse oximeter or blood gas analysis) should also be assessed regularly.

References

- 1. Prowle J R et al (2010). Fluid balance and acute kidney injury, *Nat Rev Nephrol* **6**(2): 107-115.
- 2. Segev G et al (2013). A retrospective study of acute kidney injury in cats and development of a novel clinical scoring system for predicting outcome for cats managed by hemodialysis, *J Vet Intern Med* **27**(4): 830-839.
- 3. Brown S et al (2007). Guidelines for the identification, evaluation, and management of systemic hypertension in dogs and cats, *J Vet Intern Med* **21**(3): 542-558.
- 4. McClellan J M et al (2006). Effects of administration of fluids and diuretics on glomerular filtration rate, renal blood flow, and urine output in healthy awake cats, *Am J of Vet Res* **67**(4): 715-722.
- 5. Flournoy W S et al (2003). Pharmacologic identification of putative D1 dopamine receptors in feline kidneys, *J Vet Pharmacol Ther* **26**(4): 283-290.
- 6. Halpenny M et al (2001). Effects of prophylactic fenoldopam infusion on renal blood flow and renal tubular function during acute hypovolemia in anesthetized dogs, *Crit Care Med* **29**(4): 855-860.
- 7. Connally H E et al (2010). Safety and efficacy of high-dose fomepizole compared with ethanol as therapy for ethylene glycol intoxication in cats, *J Vet Emer and CritCare* **20**(2): 191-206.
- 8. Tart K M and Powell L L (2011). 4-Methylpyrazole as a treatment in naturally occurring ethylene glycol intoxication in cats, *J Vet Emer and Crit Care* **21**(3): 268-272.

Panel 1. Treatment protocols for ethylene glycol toxicity

Ethanol is one of the traditional treatment options for ethylene glycol toxicity in cats. Its mode of action is to compete with ethylene glycol for metabolism with alcohol dehydrogenase, which has a greater affinity for ethanol than ethylene glycol. It is only considered to be effective if administered within 12 hours of ingestion. It is important to monitor mentation of cats, which should be sedated, but not comatose. The following protocol can be used for administering ethanol to exposed cats:

Dilute ethanol to 20 per cent solution (200mg/ml) in 0.9 per cent NaCl

Day 1: Give 5ml/kg IV at 0, 6, 12, 18 and 24 hours

Day 2: Give 5ml/kg IV at 8, 16 and 24 hours

Day 3: Give 5ml/kg IV at 8 hours (final treatment)

Fomepizole (or 4-methylpyrazole) is an alcohol dehydrogenase inhibitor that prevents metabolisation of ethylene glycol. However, to be effective, it must be administered within three hours of ethylene glycol toxicity[7]. It is also very expensive and not widely available within the UK. Its use has been reported in a case series of three cats in US using the following dosage[8]:

Initial dose: 125mg/kg IV

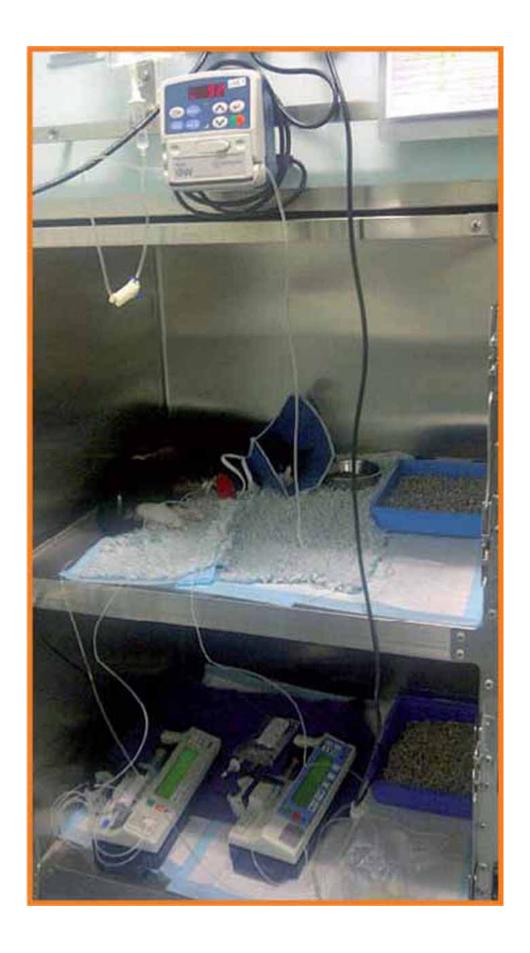**At 12, 24, 36 hours following initial dose: 31.25mg/kg IV**

Figure 1. Drip pumps and syringe drivers are invaluable for ensuring accurate fluid delivery to cats.

Figure 2. A cat undergoing renal replacement therapy with intermittent renal haemodialysis at the University of Pennsylvania School of Veterinary Medicine.

Drug	Dose	Route of administration
Calcium gluconate 10 per cent	0.5ml/kg to 1.0ml/kg	IV
Insulin	0.2IU/kg to 0.5IU/kg	IV
Dextrose	0.25g/kg to 0.5g/kg or 1g/IU to 2g/IU insulin and continued infusion of 5% dextrose with insulin)	IV
Sodium bicarbonate	1mEq/kg to 2mEq/kg	IV

Table 1. Drugs for management of hyperkalaemia and recommended dosages

Drug	Dose range	Route	Frequency
Furosemide	2mg/kg to 5mg/kg 0.25mg/kg/hr to 1mg/kg/hr	IV IV	Every one hour to two hours for a maximum of three doses CRI
Mannitol 20 per cent	0.5g/kg to 1g/kg 1mg/kg/min to 2mg/kg/min	Slow IV IV	Every hour for a maximum of two doses CRI

Table 2. Drugs for promoting diuresis and recommended dosages