Rachel Sibbald RVN C&G Cert VNES, BSAVA Merit Award (Exotics)

Rachel is a Registered Veterinary Nurse practicing in general practice in Edinburgh. She achieved the City and Guilds certificate in nursing of exotic species and has a keen interest in rabbit anaesthesia and nursing. She writes quarterly for the Rabbit Welfare Association and is currently studying towards an NCert (Anaesthesia) and the RCVS Certificate in Advanced Veterinary Nursing.
Email: rachel.sibbald@abercornvets.co.uk

Chronic renal failure in rabbits

Rachel Sibbald **RVN C&G Cert VNES, BSAVA Merit Award (Exotics)**

VetPartners Ltd, Abercorn Veterinary Clinic, Edinburgh, Scotland

ABSTRACT: This article will explore chronic renal disease in rabbits. Renal insults can be acute or chronic and can pose life threatening disease and diminished quality of life to our rabbit companions. As Veterinary Nurses it is vital we understand and recognise symptoms of disease in a variety of species so that species specific care can be employed to ensure optimum patient care and owner compliance.

Keywords: azotaemia; chronic; kidneys; rabbits; renal

Introduction

Chronic renal failure (CRF) is a common condition identified in canine and feline medicine, particularly in the geriatric population. Anatomically, most mammal kidneys are structurally similar however the physiology of renal function varies between species. Thanks to advances in rabbit medicine and surgery rabbits now have greater opportunity to become geriatric and with this life stage comes the potential for development of chronic disease.

Anatomy

The rabbit possesses a pair of unipapillate (all the collecting ducts converge to one point) kidneys with extensive evaginations of the pelvis into the medullary tissue (Varga, 2014). In wild rabbits, different environmental conditions have resulted in renal adaptation with long medullary regions being developed over generations in arid conditions and short medulla in green conditions (Meredith, 2014). The kidneys are usually the classic 'bean' shape, with the right kidney being located more cranial than the left in the abdomen. A single ureter arises from each kidney and empties into urinary bladder. The microscopic structure of the kidney is much the same as in feline patients except for the collecting ducts. The urinary bladder is thin walled but is functionally and anatomically similar to the cat and dog (Girling & Fraser, 2009).

Calcium metabolism

Rabbits have an unusual calcium metabolism and serum calcium concentration is approximately 30-50% higher than in other mammalian species. However, phosphorous and ionised calcium levels are rigidly controlled (Johnson, 2009). The intestinal absorption of calcium is directly proportionate to the amount ingested in the diet rather than metabolic need. Similarly, urinary calcium excretion increases parallel to dietary intake. The fractional excretion of calcium via the urinary tract is approximately 2% in most mammals however this can range from 45-60% in the rabbit (Wesche, 2014). When the reabsorptive capacity of the kidney is reached, calcium precipitates as calcium carbonate causing 'sludgy urine'. When metabolic demand is increased by the likes of pregnancy, less calcium is excreted via the urine and the urine may appear clear. Table 1 highlights the rabbits unique hormonal feedback regulation of calcium which differs from canine and feline patients.

Causes of chronic renal failure

The most common causes of chronic renal insult to the rabbit according to Mancinelli and Lord (2014) are listed below;

Hypercalcaemia

Paradoxically this can be caused by CRF. Hypercalcaemia can lead to mineralisation of soft tissues, particularly the kidney and this causes nephron damage (Harcourt-Brown, 2007). Uroliths can cause transient or permanent urinary outflow obstruction damaging kidneys further. Hydronephrosis, hydroureter and renomegaly may be seen in association with uroliths.

DOI: 10.1080/17415349.2020.1742828

This article has been republished with minor changes. These changes do not impact the academic content of the article.

Encephalitozoon Cuniculi

This protozoan parasite can cause granulomatous interstitial nephritis and fibrosis resulting in CRF. Typical kidney lesions manifest as depressed scars on the outer surface of the kidney. Treatment with Fenbendazole can be used to help eradicate the parasite but any renal damage will not be reversed.

Pasteurella Multocida and *Staphyloccocus* spp

These are the most common bacterial causes of pyelonephritis in the rabbit which if untreated can lead to CRF.

Renal fibrosis

Causes destruction of nephrons and calcification of the kidney, which is common in older rabbits.

Lymphoma

Multiple organs are often involved, including the kidney.

Renal hypertension

Causes renal insufficiency through systemic hypertension and impairment of renal blood flow.

Polycystic kidneys

Many rabbits show signs of CRF by 2-3 years. This causes interstitial fibrosis of the cortex and/or medulla and alterations in the Bowman's capsule.

Table 1. Hormonal feedback regulation in rabbits.

Hormone	Effect on calcium concentration in the rabbit
Parathyroid hormone (PTH)	Ionised calcium concentration is protected from hypo and hypercalcaemia by rapidly changing PTH. Despite having higher serum concentration of calcium, rabbits have readily measurable levels of PTH which can be reduced by infusion of calcium. This implies the parathyroid gland actively contributes to calcium homeostasis in this species.
Calcitonin	The physiologic effect of calcitonin in the rabbit is unclear. No consistent effect has been demonstrated.
Vitamin D	Vitamin D deficient rabbits show no detectable changes in serum calcium levels. Chronic vitamin D deficient rabbits showed no change in intestinal absorption of calcium, but excretion of calcium was decreased. This implies calcium absorption is vitamin D independent in the rabbit. This may be because calcium can absorb passively via intestinal mucosa.
Testosterone and progesterone	Both enhance reabsorption in the kidney
Growth Hormone	Enhances calcium reabsorption in the kidney

Adapted from (Johnson, 2009).

Table 2. Reference ranges for renal performance in rabbits.

Clinical parameter	Normal value	Notes
Urine specific gravity	1.003-1.036	There is wide variability in this value dependent on the rabbits' diet and is not as useful as in cats and dogs to assess concentrating ability
Urine output	20-350ml/kg/day	Huge variation dependent on diet
Urine protein:creatinine ratio	0.11-0.4	Persistent proteinuria with an inactive sediment is indicative of tubular or glomerular disease. UPC can be used to monitor disease progression in rabbits
Urine blood (dipstick)	Negative	May indicate renal infarcts, uroliths
Urine sediment	Calcium carbonate, oxalate and struvite crystals may be seen.	No RBC's, WBC's, bacteria, renal casts or proteinaceous material should be seen
Water intake	50-150ml/kg	Largely dependent on diet
Blood pressure	92-135mmHg	Needs interpreted carefully as this can reach 280mmHg in certain clinical situations
Serum urea	6.14-8.36mmol/L	Increases once 50-70% of renal function lost
Serum creatinine	44-229µmol/L	Relatively insensitive in rabbits so a rise in urea alone does not distinguish pre-renal from renal failure
Serum calcium	2.8-3.7mmol/L	This can reach >4mmol/L in healthy rabbits' dependent on dietary intake
Serum potassium	3.5-7mmol	May be increased with the use of ACE-inhibitors
Serum inorganic phosphate	1.28-1.92mmol	Increase associated with CRF indicates the loss of >80% functioning tubules
Packed cell volume	30-40%	Non-regenerative anaemia a common feature of chronic disease
Serum total protein	49-71g/l	Increase common with dehydration

*Reference ranges adopted from (Varga, 2014) and (Wesche, 2014).

Clinical signs and diagnosis

As rabbits are prey species signs of disease may be harder to detect, particularly chronic disease as the animal has time to adapt and alter their behaviour slowly over time. In rabbits' clinical signs are often mild for much of the disease process. Clinical signs noted by the owner may include; weight loss, polydipsia/polyuria, haematuria, lethargy, an unkempt coat, the presence of parasites (indicating immune compromise), reduction/cessation of playing, reduced appetite or secondary signs of gastrointestinal disease. Intermittent anorexia and ileus are a common feature of CRF. Rabbits may also sit near their water source where normally they would rest elsewhere. Rabbits attending the veterinary clinic may appear withdrawn, have poor body condition scores, signs of dehydration and abdominal palpation may reveal small and irregular kidneys (Figure 1).

To diagnose CRF the Veterinary Surgeon (VS) may perform similar tests used in canine and feline practice. Table 2 highlights common parameters used to measure renal function along with normal reference ranges.

Alongside assessing clinical parameters, the VS may use imaging. Radiography is useful to detect the presence of uroliths and urinary sludge (see Figure 2). Ultrasonography can more accurately assess renal architecture and typically the picture is of diffuse hyperechoic renal cortices with loss of corticomedullary junction (Mancinelli & Lord, 2014). Advanced imaging using commuted

Figure 1. Post mortem appearance of kidneys in a rabbit with CRF. The kidney on the left is pale and shrunken, consistent with advanced disease.

Figure 2. Lateral x-ray of 2-year-old MN rabbit with CRF. This rabbit had bilateral renal urolithiasis and severe urinary 'sludge' in both kidneys.

Figure 3. Rabbit friendly hospitalisation kennel with large hide, room to exercise and a selection of familiar foods.

tomography is particularly useful if planning surgery for urolith removal and ultrasound guided fine needle aspiration can be used to diagnose renal tumours/infection.

Treatment and nursing care

Fluid balance and correction of dehydration are paramount. Rabbits may be treated on an in or outpatient basis dependent on clinical condition and diagnosis. Stress plays an important part in rabbit disease and Brod & Sirota (1949) suggested that adrenaline is responsible for a marked and prolonged reduction in renal plasma flow and glomerular filtration rate. This is of concern when nursing the rabbit renal patient. Reduction in stress may be achieved by housing the species in a predator free ward, providing a hide and familiar food items (Figure 3). Subcutaneous (SC) fluid therapy is usually well tolerated by rabbits and the technique is easy to perform. RVN's may teach owners how to administer SC fluids at home for outpatients. A butterfly needle attached to a syringe appears to be better tolerated than a needle and syringe in the authors opinion and relatively large volumes can be administered at one time (approximately 30 mls/kg) in several different sites. Nutrition and appetite management may be challenging in rabbits with repeated episodes of ileus as often gastrointestinal stasis requires to be treated in a hospital setting. Ensuring the rabbit receives good quality fibre to stimulate gut motility is essential. Some rabbits may tolerate daily syringe feeding with convalescing formulas and these will aid gastrointestinal motility and hydration. Strong smelling food items like herbs will often stimulate feeding and freshly picked grass/dandelions are usually of interest in all but the sickest animals. Fresh greens and pellets may be soaked to increase water intake. The CRF rabbit should be offered water in a bowl (and bottle if used to this) as studies have demonstrated rabbits prefer to drink from bowls as they allow a larger intake of water in a shorter period (Tschudin et al., 2011).

Pain management may be required in cases with concurrent disease or where uroliths are causing discomfort. Many rabbits may suffer concurrent pododermatitis as a result of reduced mobility. Non-steroidal anti-inflammatories are one of the most common forms of analgesia prescribed to rabbits under the cascade as no other products are licenced. Gowan et al. (2011) found that in feline patients with International Renal Interest Society (IRIS) staging of 1, 2 and 3 the use of meloxicam for >6 months did not result in deleterious effects on renal performance. At this stage no comparative evidence is available for domestic rabbits therefore the use of NSAIDs in renal patients should be exercised with caution. Alternative analgesia may include the use of tramadol or gabapentin.

If anaemia is present, erythropoietin alpha or anabolic steroids may be administered to stimulate red cell production (Mancinelli and Lord, 2014). Anabolic steroids may also improve appetite and reduce catabolism. Ace-inhibitors may be considered in cases with proteinuria and/or systemic hypertension however rabbits appear to be highly sensitive to the hypotensive effects of benazepril therefore regular monitoring of blood pressure, urea, creatinine and electrolytes are advised (Morissey & Carpenter, 2012). Prophylactic treatment for gastric ulceration may be advisable as stress induced ulceration as a result of the stress of disease may occur in rabbits (Hinton, 1980).

Conclusion

Understanding and recognising chronic disease in rabbits can pose a challenge to both owners and veterinary professionals, however extrapolation from other species together with species specific knowledge should aid veterinary professionals when determining the best way to manage CRF in the rabbit. VN's are invaluable to rabbit patients, as good nursing care and an understanding of the species can make a huge impact in patient wellbeing, client satisfaction and the ultimate outcome in hospitalised patients.

ORCID

Rachel Sibbald http://0000-0003-1741-2434

References

Brod, J., & Sirota, J.H. (1949). Effects of emotional disturbance on water diuresis and renal blood flow in the rabbit. *American Journal of Physiology-Legacy Content*, *157*(1), 31–39. https://doi.org/10.1152/ajplegacy.1949.157.1.31

Girling, S., & Fraser, M. (2009). Anatomy and Physiology. In M. Fraser & S. J. Girling (Eds.), *Rabbit medicine and surgery for veterinary nurses* (pp. 26). Wiley Blackwell.

Gowan, R. A., Lingard, A. E., Johnston, L., Stansen, W., Brown, S. A., & Malik, R. (2011). Retrospective case – control study of the effects of long term dosing with meloxicam on renal function in aged cats with degenerative joint disease. *Journal of Feline Medicine and Surgery* , *13*(10), 752–761. https://doi.org/10.1016/j.jfms.2011.06.008

Harcourt-Brown, F. (2007). Radiographic signs of renal disease in rabbits. *Veterinary Record*, *160*(23), 787–794. http://dx.doi.org/10.1136/vr.160.23.787

Hinton, M. (1980). Gastric ulceration in the rabbit. *Journal of Comparative Pathology* , *90*(3), 475–481. https://doi.org/10.1016/0021-9975(80)90017-1

Johnson, D. (2009). *Rabbit calcium metabolism, "bladder sludge" and urolithiasis*. Retrieved October 6, 2019, from veterinary-calender.dvm360.com.

Mancinelli, E., & Lord, B. (2014). Urogenital system and reproductive diseases. In A. Meredith, & B. Lord (Eds.), *BSAVA Manual of Rabbit medicine* (p. 195). British Small Animal Veterinary Association.

Meredith, A. (2014). Biology, anatomy and physiology. In A. Meredith, & B. Lord, *BSAVA Manual of Rabbit medicine* (p. 9). British Small Animal Veterinary Association.

Morissey, J. K., & Carpenter, J. W. (2012). Therapeutics. In K. E. Quesenberry, & J. W. Carpenter (Eds.), *Ferrets, rabbits and rodents* (3rd ed., pp. 566–575). Elsevier.

Tschudin, A., Clauss, M., Codron, A., Liesegang, A., & Hatt, J.-M. (2011). Water intake in domestic rabbits (Oryctolagus cuniculus) from open dishes and nipple drinkers under different water and feeding regimes. *Journal of Animal Physiology and Animal Nutrition*, *95*(4), 499–511. https://doi.org/10.1111/j.1439-0396.2010.01077.x

Varga, M. (2014). Clinical pathology. In M. Varga (Ed.), *Textbook of rabbit medicine* (2nd ed., 114–120). Elsevier

Varga, M. (2014). Urogenital diseases. In M. Varga (Ed.), *Textbook of rabbit medicine* (2nd ed., 405). Elsevier.

Wesche, P. (2014). Clinical pathology. In A. Meredith, & B. Lord (Eds.), *BSAVA Manual of Rabbit medicine* (p. 130). British Small Animal Veterinary Association.