

The Unique Feline

Cats have a higher requirement for protein and amino acids than other species. When nutrition is inadequate, energy is derived from mobilization of amino acids from muscle stores as opposed to fat (Chan 2009). Elderly cats are also unique in comparison to other species as they have a stable to increased level of metabolism, as opposed to decreased metabolism (Laflamme 2005). A reduced ability to digest protein and fat has been documented in elderly cats. These combined factors make the utilization of high quality, easily digestible food products critical for these patients (Sparkes 2011). Cats are also particularly sensitive to changes in environmental factors, such as the timing and location of feeding, as well as the food type; smell and “mouth feel” may also play into their willingness to eat (Michel 2001).

Nutrition and Diet in Chronic Kidney Disease (CKD)

Several studies have documented the therapeutic value of a specially formulated diet in the management of CKD, including decreased incidence of uremic crisis and increased survival (Geddes et al. 2013; Ross et al. 2006). These diets typically contain conservative amounts of high quality protein, adequate non-protein calories, and are restricted in phosphorus. The failure of the patient to eat the diet negates the benefit of dietary management, and, therefore, a key therapeutic target for these patients is the maintenance of appetite and food intake. Cats with CKD often suffer from poor appetite, and, although renal diets contain adequate dietary protein, the animal will be protein deficient if not eating its caloric requirement. Management of long-term hyporexia is important. Poor body condition is associated with decreased prognosis in several species and has a negative effect on immune function, wound healing, and strength (Chan 2009). Additionally, poor appetite is perceived by owners as a significant quality of life concern and anorexia in companion animals can cause emotional distress to owners (Reynolds et al. 2010).

Does “Uremic Gastritis” Exist in CKD Cats?

Cats with CKD have been shown to have elevated concentrations of gastrin that increase with the severity of renal failure (Goldstein et al. 1998), but the relationship between gastrin, gastric acid secretion, and gastric pathology has not been investigated. The presence of gastric acid results in negative feedback to decrease the secretion of gastrin. In humans and dogs, gastrin is excreted by the kidneys, and it is hypothesized that as renal function declines, hypergastrinemia develops, resulting in gastric hyperacidity (Goldstein et al. 1998). Cats that have gastrin-secreting tumors with levels of hypergastrinemia similar to those found in cats with CKD have significant gastric pathology; however, no study has shown this to be the case in cats with CKD (Liptak et al. 2002). Even in humans, the development of hyperacidity in association with CKD appears to be inconsistent, and may be related to the presence of *Helicobacter* spp. infection (El Ghonaimy et al. 1985). Thus, there is very little available evidence on which to base recommendations for the use of acid-reducing medications such as H₂ blockers, proton pump inhibitors, or sucralfate in cats with uremia (Bartges 2012; Polzin 2011; Polzin et al. 2009; Roudebush et al. 2009).

A recent study evaluated the type and prevalence of histopathologic lesions in the stomach of cats with CKD. Cats with CKD appear more likely to have gastric fibrosis and mineralization, rather than the uremic gastropathy lesions previously described in dogs and humans. Therefore, the administration of gastric protectants such as sucralfate may not be justified, unless obvious clinical evidence of gastrointestinal hemorrhage such as melena or hematemesis is appreciated. The notable frequency of gastric mineralization, presumably as a consequence of metastatic mineralization, may highlight the need for more aggressive control of hyperphosphatemia and renal secondary hyperparathyroidism in cats with CKD. Gastrointestinal symptoms in these animals may not necessarily be the result of gastric lesions, but perhaps the consequence of circulating uremic toxins interacting with the chemoreceptor trigger zone in the brain. Medical management of gastrointestinal symptoms with anti-emetic and anti-nausea drugs may therefore be more appropriate. The exact role of hypergastrinemia in contributing to gastric hyperacidity and/or gastric lesions in cats with CKD is still unclear.

Therapies

Medical Management of Underlying Disease

Whenever possible, it is obviously ideal to address the underlying disease condition. However, in some chronic diseases, i.e., kidney disease, this is not possible and therefore medical management of complications of the chronic

disease is ideal. Dehydration and anemia can both potentially play a role in inappetence and, therefore, should be addressed when applicable.

Environmental Factors and Food Choices

As cats are particularly sensitive to environmental factors, suggestions for appetite enhancement include: a quiet environment with exclusive access to food without interference from bothersome household members; novel food type in cases of possible aversion; similar food type in case of food exclusivity; warming the food, particularly if olfaction is an issue, or, alternatively, chilling the food if aromas appear to result in nausea; social interaction while eating; feeding small frequent meals as premature satiety is associated with many disease states.

Pain Management

For both acute and chronic medical conditions, appropriate management of pain is critical to improving appetite. Opioids are perhaps most commonly utilized. Buprenorphine has a significantly longer half-life and may be useful for in home palliation of chronic pain. Butorphanol may also have some visceral analgesic properties. Opioids should be used with caution in patients with ileus. Maropitant may also have some visceral analgesic properties (Boscan et al. 2011).

Anti-nausea Therapy

Cats with CKD likely suffer from nausea, vomiting, and inappetence as a result of uremia—a buildup of toxins in blood—that affects the chemoreceptor trigger zone in brain. In addition, uremia may have effects on the intestinal tract that lead to further unwillingness to eat. Several anti-nausea therapies have become recently available. These include maropitant, ondansetron, and dolasetron. These drugs work at the nausea center in the brain as well as in the gut and can be given as an injection. Ondansetron has been documented to be helpful in human patients suffering from uremia (Ljutic et al. 2002). However, recent pharmacokinetic studies in cats have demonstrated that oral bioavailability of ondansetron is poor in cats (~35%) and the half-life is very short (approximately one hour) making it a q 8hr medication (Quimby et al. 2013). Subcutaneous ondansetron has a slightly longer half-life of three hours. In addition to its appetite-stimulating properties, mirtazapine demonstrates anti-nausea properties as it acts at the 5HT₃ receptor similarly to ondansetron and dolasetron (Quimby and Lunn 2013; Riechelmann et al. 2010). Limiting gastric acidity with the use of H₂ blockers or proton pump inhibitors such as famotidine or omeprazole, respectively, anecdotally appears to palliate inappetence in some patients; however, as previously mentioned, both the degree of hyperacidity present in CKD and the efficacy of these medications for management of cats with CKD remains unproven. Recent studies of the effect of omeprazole on the gastric pH in cats indicates that it is superior to famotidine in its ability to inhibit acid production and twice daily dosing may be necessary (Tolbert 2014).

Cerenia Clinical Trial: Cerenia is commonly used for acute vomiting. A pharmacokinetic and toxicity study in cats indicated that longer-term usage appears safe (Hickman et al. 2008). A recent study assessed the efficacy of Cerenia for management of chronic vomiting and inappetence associated with feline CKD (Quimby et al. 2014). When given daily for two weeks, Cerenia was demonstrated to palliate vomiting associated with CKD; however, it did not appear to significantly improve appetite or result in weight gain in cats with Stage II and III CKD within the timeframe of the study.

Appetite Stimulant Therapy

Cyproheptadine has been used for some time as an appetite stimulant and has anecdotal efficacy in many patients; however, its efficacy has never been scientifically evaluated. Twice daily administration is necessary in many cases and this can prove a challenge for owners, particularly long-term. Sedation is a common side effect. Mirtazapine has become more commonly used and recent exploration of its pharmacodynamics and pharmacokinetics has provided information for more effective use in cats (Quimby et al. 2011a; Quimby et al. 2011b). Pharmacodynamic studies have illustrated that it can be a potent appetite stimulant, but higher doses are more commonly associated with side effects (hyperexcitability, vocalization, tremors). Smaller, more frequent doses are recommended. The half-life is short enough that it could be administered daily in normal cats. Renal disease delays clearance and in these patients, every other day administration is recommended (Quimby et al. 2011a). Owners should be aware that mirtazapine and cyproheptadine cannot not be administered concurrently; cyproheptadine is in fact used as an antidote for the serotonin effects of a mirtazapine overdose.

Mirtazapine Clinical Trial: A recent placebo-controlled, double-masked crossover clinical trial was performed to evaluate the effects of mirtazapine on body weight, appetite, and vomiting in cats with CKD (Quimby and Lunn

2013). Mirtazapine is an effective appetite stimulant in cats with CKD and resulted in significantly increased appetite and weight. Mirtazapine also appears to have anti-emetic properties and resulted in significantly decreased vomiting in cats with CKD. This drug could be a useful adjunct to the nutritional management of cats with CKD.

Commonly Used Appetite Stimulant and Anti-nausea Medications

Drug	Receptor	Location of action	Dosage
Butorphanol	ENK	Cerebral cortex and CRTZ	0.2–0.4 mg/kg SQ, IV q 6-8 hrs
Buprenorphine	<i>mu</i>	Various	0.005–0.01 mg/kg SQ, buccal mucosa
Metoclopramide	D2 (weak)	CRTZ (weak)	0.2–0.4 mg/kg SQ, IV q 6-8hrs
Ondansetron	5HT3	CRTZ and GI afferent	0.5–1.0 mg/kg IV, SQ, p.o. q 8 hrs
Dolasetron	5HT3	CRTZ and GI afferent	0.6–1.0 mg/kg IV, SQ, p.o. q 24hrs
Maropitant	NK-1	Emetic center, CRTZ, GI	1 mg/kg SQ, p.o. q 24hrs
Mirtazapine	5HT3	CRTZ and GI afferent	1.87mg q 24 hrs in normal cats, q 48 hrs in cats with kidney disease.
Cyproheptadine	H1	Various	2–4 mg per cat q 12–24 hrs

Learned Food Aversion

Care should be taken to select the appropriate patients for appetite enhancement as learned food aversion is thought by most to be prevalent in cats (Michel 2001). Learned food aversion occurs when the patient associates nausea, pain, or other physical manifestations of disease with the act of eating or the sight or scent of food. Even after the underlying illness is resolved, this aversion may remain. Therefore, it is critical that cats that are overtly nauseous—drooling, gagging, turning away from food—particularly in hospital or in acute illness, are not forced to eat lest food aversion be created (Michel 2001).

If cats are too nauseous or critical to even consider oral feeding, or have not responded to appetite encouragement after three to five days, placement of an enteral feeding tube should be considered. Nasoesophageal, esophageal, or gastrostomy tube can be chosen depending on the type and duration of feeding desired (Chan 2009). Esophageal feeding tubes can be a valuable tool for long-term management of CKD patients as food, medications, and water can be easily given without stressing the patient. Parenteral feeding should be considered in cats that cannot tolerate enteral feeding. Additionally, many clinicians feel that prescription diets (i.e., renal) should not be fed in hospital during a crisis lest an aversion be created to the diet desired for long-term management. The best candidates for pharmacological enhancement of appetite are cats leaving the hospital with their acute crisis resolved and cats with a chronic disease in the home environment.

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