

PANCREATITIS IN CATS: MANAGEMENT OF A COMPLICATED DISEASE

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Feline pancreatitis is a very difficult disease to definitively diagnose antemortem (especially chronic cases or in cats that do not vomit) and treatment remains symptomatic and supportive. This is partly due to the lack of specific clinical signs in cats, as well as the lack of a rapidly available test for diagnosis of the disease – and in cats with chronic pancreatitis, testing is still very difficult. This talk will review the salient features of both acute and chronic pancreatitis in cats and discuss the treatment of cats with pancreatitis – a problem intensified by the complications that develop in anorectic cats.

Diagnosis

The clinical signs of feline pancreatitis are quite different from those in dogs. Acute pancreatitis is frequently encountered in obese dogs fed a high fat diet, while cats are more likely to be underweight, and high fat diets do not appear to be an important predisposing factor. Cats of all ages, sexes and breeds are affected, although Siamese cats are reported to have pancreatitis more frequently. Finally the clinical signs of pancreatitis in cats are more vague, with the most common signs being lethargy (reported in 100% of cats in one study), anorexia, dehydration and abnormal body temperature (either fever or hypothermia can be observed). Vomiting and anterior abdominal pain, which are common clinical signs in dogs with acute pancreatitis, occur in only 35% and 25% of cats, respectively. Cats with severe necrotizing pancreatitis may be icteric or in shock. Other conditions that may occur concurrently with pancreatitis in cats include hepatic lipidosis, cholangiohepatitis, inflammatory bowel disease, interstitial nephritis, diabetes mellitus or vitamin K responsive coagulopathy. Thus, the clinical signs may be quite variable, and this must be taken into consideration with each patient. In addition, with increases in liver enzymes and bilirubin, the signs and abnormalities can easily be attributed to liver dysfunction, which further delays the diagnosis.

Routine evaluation of cats with suspected pancreatitis may include hematology, a serum biochemistry profile, urinalysis, abdominal radiography and/or ultrasound, and serum assays of pancreatic function (e.g. feline trypsin like immunoreactivity –fTLI, or feline pancreatic lipase immunoreactivity – fPLI). Hematologic findings in cats with pancreatitis are nonspecific, but may include a nonregenerative anemia, leukocytosis or leukopenia (less common). In a recent study, cats with pancreatitis consistently had an elevated WBC (20,300 cell/uL) and mild decreases in platelets (mean = 180,000 platelets/ul). Reported changes in the serum chemistry profile include elevated serum alanine aminotransferase (ALT), elevated serum alkaline phosphatase (ALP), hyperbilirubinemia, hyper- or hypcholesterolemia, hyperglycemia, azotemia, and hypokalemia. In a recent study, the most common abnormalities in cats with severe pancreatitis were hyperglycemia (180 mg/dL), hyperbilirubinemia (2.5 mg/dL), hypocholesterolemia (130 mg/dL), and hypoalbuminemia (1.8 g/dL). Liver enzyme elevations were more common in cats with mild pancreatitis (determined by surgical biopsy), and GGT, ALP, and ALT were all moderately elevated in these cats. Hypocalcemia is less commonly observed, but when present may be a poor prognostic sign seen in cats with severe pancreatitis or multiple organ dysfunction. Serum lipase may be increased early in acute pancreatitis, but in a recent study amylase and lipase were found to be of little diagnostic value in distinguishing normal cats from those with pancreatitis. There are no changes in the urinalysis consistently observed or specific for pancreatitis in cats.

The fTLI was developed years ago as the definitive test for diagnosis of exocrine pancreatic insufficiency, and the data and follow up have confirmed its utility for this condition. In recent years, others have evaluated the fTLI as a diagnostic test for acute pancreatitis –

working on the premise that an elevation in serum concentrations were consistent with pancreatic leakage or inflammation. While an increase in fTLI can be found in cats with acute pancreatitis, a normal fTLI does not rule out pancreatitis. This is because the leakage of enzymes tends to decrease or are controlled by the body's peptidases (macroglobulin, etc) within 12-24 hours following an acute insult. Further, in chronic or low grade pancreatitis, the leakage is not great enough to be detected by this assay. Thus, while an increase in fTLI is specific for pancreatic enzyme leakage, it is not sensitive enough to be a definitive test for pancreatitis. More recently, an ELISA for pancreatic specific lipase (feline pancreatic lipase immunoreactivity –fPLI) was developed by the GI lab at Texas A&M University. The assay is species specific, has been used to detect elevations in pancreatic lipase in clinical cases, and appeared to be more specific and sensitive for diagnosis of pancreatitis in cats than fTLI. However, the assay had a relatively low sensitivity (33%) and specificity (<80%) when a cut off value of 100 ug/L was used for diagnosis. To improve upon this assay, a radioimmunoassay (RIA) was developed and validated in 30 healthy cats. In a recent paper, the sensitivity and specificity of this assay was tested in cats with mild pancreatitis and in cats with moderate to severe pancreatitis. The sensitivity in mild pancreatitis was found to be 80% while the specificity in healthy cats 75%. However, in severe pancreatitis (determined by pancreatic biopsy) the sensitivity and specificity were both 100%. These findings underscore the utility of this test in cats with acute pancreatitis, however, there still is a problem with detection of low grade or chronic pancreatic inflammation in cats with this assay. In cats with chronic pancreatitis it will still be necessary to evaluate the combined historical, physical exam, lab data and imaging information along with the fPLI when making a diagnosis.

Imaging studies are frequently used to help identify cats with acute pancreatitis, however, the changes are not consistent and can be particularly subject to interpretation and operator expertise. The most common radiographic abnormalities include a generalized or focal (upper right quadrant) loss of peritoneal detail (suggesting peritonitis or peritoneal effusion), presence of a mass in the area of the pancreas, hepatomegaly, dilated intestinal loops, or a fluid-filled duodenum. However, these findings are not specific for pancreatitis, and the sensitivity of radiography for diagnosing pancreatitis is low in cats. Ultrasonography may reveal a hypoechoic pancreas, hyperechoic mesentery, a mass effect, a dilated common bile duct or it may be normal. In previous studies, the sensitivity of ultrasound for diagnosis of pancreatitis was reported to be 24%. In a recent study, mild pancreatitis was still shown to be difficult to diagnose via abdominal ultrasound. However, in that same study, ultrasound had a 80% sensitivity and 88% specificity in cats with moderate to severe pancreatitis. In humans, the "gold standard" for a noninvasive diagnosis of pancreatitis, but in this study, only 2 of the 10 cats showed evidence consistent with pancreatitis and there was large variability in the ability of this imaging technique to assess pancreatic size. As such, the cost, availability, the difficulties in imaging the normal feline pancreas using CT, make this method less attractive and unrealistic for use in the diagnosis of feline pancreatitis. The most reliable method for making an accurate diagnosis of pancreatic disease remains direct visualization and histopathology. However, this can be expensive, increase the risk of complications (anesthesia/surgery), and in cases with focal lesions, the lesions may be missed on visual or histopathologic inspection.

Treatment of Pancreatitis

Acute pancreatitis in cats can be a significant therapeutic challenge. As with the treatment of dogs, the therapy is supportive and aimed at restoring circulating blood volume while allowing the pancreas to "rest". If an inciting cause can be identified, it should be corrected; however, greater than 90% of cases are idiopathic. The mainstay of treatment is aggressive fluid therapy, and if the cat is vomiting, withholding food and water for 2-3 days. Colloid support can be obtained with hydroxyethyl starch (Hetastarch) or plasma if it is available.

Plasma can be especially beneficial, as it provides additional alpha macroglobulins which are important scavengers of pancreatic enzymes. If the cat is unable to tolerate water or food after the 2-3 day period, alternative routes of nutritional support must be considered to prevent development of hepatic lipidosis or protein/calorie malnutrition and immunosuppression. The preferred method of nutritional support for cats with severe pancreatitis is via a jejunostomy (J) tube, but this requires an invasive procedure and may not be possible in all cats. Partial or total parenteral nutrition are viable alternatives. If the cat is not vomiting, placement of an esophagostomy (E) or percutaneous endoscopic gastrostomy (PEG) tube are reasonable alternatives – especially in cats with known or suspected hepatic lipidosis as a concurrent problem. The key point is this: you can't starve cats with pancreatitis – if they are not vomiting, use low fat enteral nutrition and “feed through” the pancreatitis. In cats with chronic, low grade pancreatitis this is even a more important aspect of long term management.

One aspect of therapy that must be considered in cats with pancreatitis is pain management (whether or not they show overt pain this is important). Careful palpation in most cats will reveal cranial quadrant pain in cats with significant pancreatic inflammation. Pain relief can be achieved with buprenorphine (0.005-0.01 mg/kg IV, or IM q 4-8 hr), meperidine (1-2 mg/kg IM q2-4 hr), or butorphanol (0.2-0.4 mg/kg IM q2-4 hr). In addition, low dose CRI ketamine or lidocaine infusions are effective in reducing somatic pain, and lidocaine at these low doses has prokinetic activity. Morphine should be avoided as it can cause pancreatic duct spasm.

Other aspects of supportive therapy to consider are antibiotic therapy, control of vomiting, use of pancreatic enzymes, anti-coagulants (for cats in DIC), and finally, anti-inflammatory (steroid) therapy. Antibiotic therapy is generally indicated in all cats with severe pancreatitis, anorexia for long periods, or in cats with systemic inflammatory response syndrome (SIRS) as the risk of bacterial translocation and secondary sepsis are considerable. In general, broad spectrum antibiotics that cover intestinal aerobes and anaerobes should be chosen. Cefotaxime at a dose of 50 mg/kg administered intramuscularly every eight hours prevents bacterial colonization of the pancreas.

- Anti-emetic agents – Nausea and vomiting may be severe in affected animals. The α_2 adrenergic antagonists and 5-HT₃ antagonists appear to be the most effective anti-emetic agents in the cat. Cats may be treated with chlorpromazine (α_2 adrenergic antagonist) at a dose of 0.2-0.4 mg/kg administered subcutaneously or intramuscularly every 8 hours, or with any of the 5-HT₃ antagonists (ondansetron 0.1-1.0 mg/kg, granisetron 0.1-0.5 mg/kg, or dolasetron 0.5-1.0 mg/kg, orally or intravenously every 12-24 hours). Dopaminergic antagonists, e.g., metoclopramide, are less effective anti-emetic agents in the cat, and because they antagonize dopamine, may potentially reduce pancreatic blood flow (this effect has not been proven in cats with pancreatitis).
- Calcium gluconate supplementation – Hypocalcemia is a frequent complication of feline acute necrotizing pancreatitis. Calcium gluconate should be given at doses of 50-150 mg/kg intravenously over 12-24 hours, along with measurement of serum total or ionized calcium concentrations to allow adjustments in therapy.
- H₁ and H₂ histamine antagonists – Histamine and bradykinin-induced increases in microvascular permeability are associated with the development of hemorrhagic necrosis in experimental feline pancreatitis. Treatment with H₁ (mepyramine, 10 mg/kg) and H₂ (cimetidine, 5.0 mg/kg) histamine receptor antagonists protects against the development of hemorrhagic pancreatitis in these feline models. Efficacy has not been established in clinical pancreatitis, but the use of these drugs in suspected or proven clinical cases seems appropriate. Diphenhydramine (2-4 mg/kg) or dimenhydrinate (4-8 mg/kg) are examples of clinically used H₁ histamine receptor antagonists. Cimetidine (5.0 mg/kg), ranitidine (1.0-2.0 mg/kg), famotidine (0.5-1.0 mg/kg), and nizatidine (2.5-5.0 mg/kg) are examples of H₂ histamine receptor antagonists.

- Low dose dopamine infusion – Low dose dopamine infusion (5 µg/kg/min) improves pancreatic blood flow and reduces microvascular permeability in feline experimental pancreatitis. Low dose dopamine infusion is effective treatment in experimental pancreatitis even when it is given up to 12 hours after induction of the disease. Part of the appeal of dopamine as a potential treatment for feline pancreatitis lies in the diversity of its actions (cardiac, renal, and systemic pressure).
- If the cat is hyperglycemic (suggesting glucose intolerance or diabetes mellitus), regular insulin should be administered (1U/kg/day via continuous IV infusion or 0.2 U/kg IM q4-6h).
- Steroid therapy was once controversial, and is not recommended in cats with acute, necrotizing pancreatitis or pancreatic abscessation. But, there appears to be increasing evidence of an association with pancreatitis and IBD in cats, and in these cases, steroid therapy is clearly indicated.
- Ductal decompression – Surgical decompression of the pancreaticobiliary duct should be considered in cases of acute ductal obstruction, e.g., calculus, neoplasia, and fluke infection. Ductal decompression has been shown to restore pancreatic blood flow, tissue pH, and acinar cell function.
- Ductal decompression may also be useful in acute cases that have progressed to the more chronic form of the disease.

The diet chosen should be highly digestible and low fat to reduce stimulation of pancreatic secretions. In some cats, a homemade, low fat diet (e.g. chicken/turkey and rice in 2:1 proportions) may be beneficial, as there are no commercially available feline diets that are both very highly digestible and very low in fat. Ultimately, the goal is to find an appropriate diet for the cat that is both commercially available and acceptable to the cat. An important point about feeding cats during this period is to avoid force feeding – not only because it is very difficult to achieve the appropriate level of caloric intake by this method, but also because it can induce food aversion.

Partial (Peripheral) Parenteral Nutrition (PPN)

Parenteral nutrition is nutrition delivered by an intravenous route. While enteral nutrition is always preferred, parenteral nutrition can be life saving in cats that cannot tolerate enteral feeding or are unable to meet their energy needs by enteral nutrition alone. Total parenteral nutrition, which allows provision of all the cat's daily nutritional needs intravenously, are hyperosmolar solutions and must be delivered through a central venous catheter. The logistics of stocking and compounding the required solutions, placement of central venous catheters and their care, and the provision of intensive patient monitoring around the clock have limited the use of total parenteral nutrition (TPN) to large practices and teaching hospitals. In recent years, major innovations in catheters (less thrombogenic and less prone to kinking) have made use of peripheral nutrition more practical and possible. While there are still drawbacks and limitations to PPN, the process has been greatly simplified.

In general: PPN is used in cats requiring nutritional support for less than one week, as it is intended to be “gap” nutrition – in other words, to fill the gap until better support (or complete support) can be provided.

Key Issues

- PPN is used to provide up to 50% of the of the patient's energy needs for 24 hr. Thus, unlike TPN, it cannot be the only source of nutritional support for a patient for more than a few days.
- PPN does not require a central venous line – only a dedicated peripheral catheter is required.

- Because the PPN catheter must not be used for other purposes to reduce the risk of sepsis, a second catheter must be placed for fluids, blood draws, etc.
- Silicone elastomer or polyurethane catheters appear to be the least thrombogenic than commonly used Teflon catheters
- Placement of the catheter as a sterile procedure is a must – PPN solutions are ideal for growth of bacteria.
- Minimize changes/opening connections – change drip sets every other day – don't reuse them with new PPN solution.
- The basic solution is a protein source (8.5% amino acid solution), a CHO source (5 % dextrose), and a fat source (20% lipid emulsion), with added vitamins, minerals and electrolytes as needed.
- The key difference for PPN versus TPN is the osmolarity of the solution. TPN is often > 1200 mOsm/L, while the goal is to keep PPN solutions < 800 mOsm/L.
- 5% Amino acid solutions < 500 mOsm/L and 20% lipid solutions are 340 mOsm/L – it is the CHO solutions used that can increase osmolarity, thus 5-10% solutions are used to reduce this problem.
- PPN solutions must be mixed under aseptic conditions and in a specific order – it is best to have them formulated by a pharmacist if possible – and they must be used within 24-36 hours once administration is started.
Order: AA + dextrose, then electrolyte and vitamin/mineral solutions, finally add lipids last – care should be taken to avoid precipitation (if it occurs, the solution must be discarded).
- Delivery of PPN solutions must be continuously via an infusion pump. Both slow initiation and slow cessation of PPN administration is essential to prevent metabolic crises (hypo/hyperglycemia, hypertriglyceridemia, etc).
- Decide the amount of calories to be administered for the patient (using the same calculations as for enteral nutrition).

Nutrient Requirements:

Cats (< 10 kg)

$IER \times 0.50$ (50% of nutrients/day) $\times 0.25$ (% kcal from dextrose) = kcal/day from dextrose

$IER \times 0.50 \times 0.25$ = kcal/day from amino acids

$IER \times 0.50 \times 0.50$ = kcal/day from lipid

Volume Requirements for Solutions

1. 5% Dextrose = 0.17 kcal/ml

$kcal/day \div 0.17$ kcal/ml = ml/day dextrose

2. 8.5% amino acid solution w/ electrolytes = 0.34 kcal/ml

$kcal/day \div 0.34$ kcal/ml = ml/day amino acids

3. 20% lipid solution = 2 kcal/ml

$kcal/day \div 2$ kcal/ml = ml/day lipid

B complex solution = 2-4 ml/L

Add each component to give the total volume (ml) of PPN solution

Total volume $\div 24$ hr = ml/hr (approximates a maintenance rate of fluid)

- The most common complications are with catheter occlusion, premature removal, line disconnection or thrombophlebitis. These problems can be minimized with proper catheter placed and patient monitoring.

- Metabolic complications with TPN are much greater than with PPN, but still must be considered. The most common complication of PPN is hyperglycemia. Hyperammonemia and hypertriglyceridemia are much less common with PPN than TPN and if they occur, require reformulation of the solution.
- Volume overload can occur in patients with congestive heart failure or renal failure, or in very small dogs or cats – intravenous fluid rates must be adjusted to account for the volume.
- The most serious complications are venous thrombosis and septicemia secondary to catheter infection or solution contamination. Any change in body temperature should be immediately assessed and addressed.