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Objective—To determine the incidence and prognostic significance of low plasma ionized calcium concentration in cats with clinical signs of acute pancreatitis (AP).

Design—Retrospective study.

Animals—46 cats with AP and 92 control cats with nonpancreatic diseases.

Procedure—Medical records were reviewed, and results of clinicopathologic testing, including plasma ionized and total calcium concentrations, acid-base values, and electrolyte concentrations, were recorded. Cats with AP were grouped on the basis of outcome (survived vs died or were euthanatized), and plasma ionized calcium concentrations, acid-base values, and electrolyte concentrations were compared between groups.

Results—Serum total calcium concentration was low in 19 (41%) cats with AP and plasma ionized calcium concentration was low in 28 (61%). Cats with AP had a significantly lower median plasma ionized calcium concentration (1.07 mmol/L) than did control cats (1.12 mmol/L). Nineteen (41%) cats with AP died or were euthanatized; these cats had a significantly lower median plasma ionized calcium concentration (1.00 mmol/L) than did cats that survived (1.12 mmol/L). Ten of the 13 cats with AP that had plasma ionized calcium concentrations ≤ 1.00 mmol/L died or were euthanatized.

Conclusions and Clinical Relevance—Results suggest that low plasma ionized calcium concentration is common in cats with AP and is associated with a poorer outcome. A grave prognosis and aggressive medical treatment are warranted for cats with AP that have a plasma ionized calcium concentration ≤ 1.00 mmol/L. (J Am Vet Med Assoc 2001;219:1105–1109)

Acute pancreatitis (AP) is regarded as a common disease in people and dogs. In the past, this disorder was considered uncommon in cats, and the diagnosis was made only at the time of postmortem examination. More recently, an increased index of suspicion and an improved ability to detect clinicopathologic and ultrasonographic evidence of this disease have led to an increase in the frequency of antemortem diagnosis of AP in cats. Hypocalcemia is associated with a poor outcome in human patients with AP; the use of a severity score based on degree of organ system compromise may have some prognostic value for dogs with AP. However, the prognostic significance of hypocalcemia in veterinary patients with AP is unknown. Hypocalcemia is apparently an uncommon finding in dogs with fatal AP, but a necropsy study has suggested that it may be common in cats with fatal AP. On the other hand, the incidence of low plasma ionized calcium concentration in cats with AP has not been determined. Therefore, the purpose of the study reported here was to determine the incidence and prognostic significance of low serum total and plasma ionized calcium concentrations in cats with AP.

Criteria for Selection of Cases

Medical records of all cats admitted to the Emergency Service of the Veterinary Hospital of the University of Pennsylvania between January 1996 and August 1998 were searched. Cats were included in the study if the following 3 criteria were fulfilled: the cat had a history of ≤ 3 weeks’ duration of clinical signs consistent with a diagnosis of AP; 1 or more ultrasonographic, pathologic, or histopathologic findings were consistent with a diagnosis of AP; and results of venous blood gas analyses and serum biochemical analyses, including determination of plasma ionized calcium concentration, performed at the time of admission were available for review. Clinical findings considered consistent with a diagnosis of AP included anorexia, lethargy, vomiting, signs of abdominal pain during physical examination, and icterus. Ultrasonographic findings considered consistent with a diagnosis of AP included hypoechoic pancreatic parenchyma or hyperechoic peripancreatic mesentery. Gross evidence of pancreatic edema, hyperemia, or hemorrhage and histologic evidence of pancreatic or peripancreatic fat necrosis or suppurative inflammation of the pancreas were considered consistent with a diagnosis of AP.

Procedures

Medical records were reviewed, and physical examination findings, serum total and plasma ionized calcium concentrations, acid-base values (venous blood pH, P, CO₂, anion gap, base excess), and serum electrolyte concentrations (potassium, sodium, and chloride) were recorded. In some cats, various other clinicopathologic tests, including CBC, urinalysis, abdominal ultrasonography, and measurement of serum total thyroxine concentration and serum trypsin-like immunoreactivity (TLI), had been performed, and results of these tests were also recorded. Cats were considered to have survived if they were discharged from the hospital and were still alive at the time of

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time of follow-up; cats that were lost to follow-up were considered to have survived. Cats were considered to have not survived if they died or were euthanatized because of a lack of response to treatment for AP or related complications during hospitalization or after discharge from the hospital.

Control cats were randomly selected from among all sick cats examined at the Emergency Service of the Veterinary Hospital of the University of Pennsylvania between January 1996 and August 1998 for any reason other than pancreatitis or any other disorder of the pancreas. For each control cat, age and plasma ionized calcium concentration were recorded from the medical record.

Statistical analyses—Values for most variables were not normally distributed. Therefore, descriptive statistics calculated for continuous variables were median and interquartile range (IQR; 25th to 75th percentile). The Wilcoxon rank sum test was used to compare values for continuous variables between case and control cats and between case cats that survived and case cats that did not survive. The Spearman rank correlation method was used to determine whether plasma ionized calcium concentration was correlated with serum total calcium, creatinine, phosphorus, potassium, sodium, chloride, albumin, glucose, or total thyroxine concentration; venous blood pH; anion gap; base excess; or P_{vCO2}. The χ² test or Fisher exact test was used to compare categorical data between groups. For all analyses, a value of P < 0.05 was considered significant.

Results

Signalment—Forty-six cats with AP met the criteria for inclusion in the study. These cats represented 0.57% of all cats examined at the veterinary hospital during the study period. Cats ranged from 9 months to 18 years old (median, 10 years; IQR, 6 to 14 years). There were 38 (83%) domestic shorthairs, 2 (4%) domestic longhairs, 2 (4%) Siamese, 1 (2%) Himalayan, 1 (2%) Abyssinian, 1 (2%) Persian, and 1 (2%) Maine Coon. Twenty-five (54%) cats were male, and 21 (46%) were female; all male cats and all but 1 female cat were neutered.

History and clinical findings—Forty-four (96%) cats had a history of decreased appetite, 38 (83%) had a history of lethargy, 20 (43%) had a history of vomiting, 18 (39%) had a history of weight loss, 9 (20%) had a history of polyuria and polydipsia, and 5 (11%) had a history of diarrhea. On physical examination, 10 (22%) cats were moderately to severely icteric, 8 (17%) had signs of abdominal pain, 5 (11%) had abdominal distension, and 2 (4%) had a palpable mass in the cranial aspect of the abdomen.

Ultrasonographic findings—Abdominal ultrasonography was performed on 42 (91%) cats. Abnormal findings included an enlarged, irregular, or hypoechoic pancreas in 27 (64%) cats (Fig 1); an enlarged or hypoechoic liver in 19 (43%); hyperechoic peripancreatic mesentery in 18 (43%); abdominal effusion in 13 (31%); distension of the gall bladder and common bile duct in 7 (17%); and thrombosis of the pancreatico-duodenal vein in 2 (5%). Results of abdominal ultrasonography were normal in 3 (7%) cats.

Pathologic findings—Three cats underwent exploratory abdominal surgery, and the pancreas was visibly hyperemic and edematous in all 3. In 2 of the 3 cats that underwent surgery, biopsy specimens were obtained. Histologic examination of these specimens revealed suppurative pancreatitis in 1 cat and necrotizing pancreatitis in the other. Histologic examination of hepatic biopsy specimens revealed hepatic lipidosis in both cats and suppurative cholangitis-cholangiohepatitis in 1.

A postmortem examination was performed on 14 cats that died or were euthanatized. Ten (71%) had peripancreatic fat necrosis, 7 (50%) had moderate to severe neutrophilic infiltration of the pancreas, and 5 (36%) had necrotizing pancreatitis (Fig 2). Five (36%) cats had hepatic lipidosis, 2 had duodenal inflammation, and 1 had thrombosis of the pancreatico-duodenal vein. Fibrosis was not observed in any of the pancreatic necropsy specimens.
CATS WITH PANCREATITIS—Nineteen of the 46 (41%) cats with AP died or were euthanatized. Of these, 4 cats died while hospitalized, and 3 died 10, 12, and 120 days after discharge from the hospital. Eight cats were euthanatized while hospitalized, and 4 were euthanatized 1, 4, 13, and 15 days after discharge because of a critical condition and grave prognosis or a lack of clinical improvement since the time of discharge. Of the 27 cats with AP that survived, follow-up information was available for 24; duration of follow-up ranged from 1 week to 2 years. The 3 cats that were lost to follow-up were included with the cats that had survived.

Plasma ionized calcium concentration was low in 28 (61%) cats with AP, including 16 of the 19 (84%) cats that did not survive and 12 of the 27 (44%) cats that did. Plasma ionized calcium concentration was ≤ 1.00 mmol/L in 10 of the 19 (53%) cats that did not survive and in 3 of the 27 (11%) cats that did. Serum total calcium concentration was low in 19 (41%) cats with AP, including 11 (58%) cats that did not survive and 8 (30%) cats that did. Median plasma ionized calcium concentration was significantly (*P < 0.003) decreased, compared with concentration for control cats (median, 1.12 mmol/L; IQR, 1.08 to 1.16 mmol/L), in cats with AP (median, 1.07 mmol/L; IQR, 0.99 to 1.15 mmol/L) and in cats with AP that did not survive (1.00 mmol/L; IQR, 0.93 to 1.07 mmol/L). However, median plasma ionized calcium concentration for cats with AP that survived (median, 1.12 mmol/L; IQR, 1.05 to 1.17 mmol/L) was not significantly different from concentration for control cats, and median concentration for cats with AP that survived was significantly higher than median concentration for cats with AP that did not survive (Fig 3). Ten of 13 (77%) cats with AP that had plasma ionized calcium concentration ≤ 1.00 mmol/L did not survive.

Compared with cats with AP that survived, cats with AP that did not survive had significantly lower median serum total calcium (8.5 mg/dl [IQR, 7.7 to 9.3 mg/dl; n = 19] vs 9.4 mg/dl [IQR, 8.8 to 9.9 mg/dl; n = 25]; P < 0.03) and serum total thyroxine (1.3 µg/dl [IQR, 0.7 to 1.6 µg/dl; n = 9] vs 1.9 µg/dl [IQR, 1.2 to 2.2 µg/dl; n = 15]; P < 0.03) concentrations. There were no significant differences between groups (cats with AP that did not survive vs cats with AP that did survive) with regard to venous blood pH (7.377 [IQR, 7.302 to 7.398; n = 19] vs 7.376 [IQR, 7.350 to 7.397; n = 26]) or serum creatinine (1.50 mg/dl [IQR, 0.95 to 2.45 mg/dl; n = 19] vs 1.3 mg/dl [IQR, 0.95 1.98 mg/dl; n = 27]), albumin (2.6 g/dl [IQR, 2.0 to 3.2 g/dl; n = 19] vs 2.8 g/dl [IQR, 2.4 to 3.2 g/dl; n = 27]), potassium (3.7 mmol/L [IQR, 3.4 to 4.3 mmol/L; n = 19] vs 4.0 mmol/L [IQR, 3.5 to 4.2 mmol/L; n = 27]), or glucose (167 mg/dl [IQR, 120 to 224 mg/dl; n = 19] vs 144 mg/dl [IQR, 117 to 225 mg/dl; n = 27]) concentration.

Plasma ionized calcium concentration was significantly correlated with serum total calcium concentration (*r = 0.54, P < 0.002), serum total thyroxine concentration (*r = 0.58, P < 0.003), anion gap (*r = -0.35, P < 0.02), serum sodium concentration (*r = 0.40, P < 0.007), serum chloride concentration (*r = 0.64, P < 0.001), and serum albumin concentration (*r = 0.55, P < 0.001).
variable delay during this period before TLI results were available to clinicians. Therefore, TLI played only a minor role in the diagnosis of AP in these cats and in treatment decisions made by the attending clinicians.

Hypocalcemia was a common finding in cats with AP in this study, and incidence of hypocalcemia appeared to be higher than the incidence in dogs. Although some cats were hypoalbuneminic and there is a significant relationship between serum albumin and serum total calcium concentrations in cats, a low ionized calcium concentration reflects a decrease in the free or active fraction of total calcium. Further, serum albumin concentration was not significantly different between cats with AP that survived and cats with AP that did not survive. With alkalemia, there is a decrease in ionized calcium concentration. However, none of the cats in this study were alkalemic. Therefore, ionized calcium concentrations would not be expected to be falsely decreased.

To our knowledge, plasma ionized calcium concentrations in cats with AP have not been reported previously. Several mechanisms have been proposed for the development of low ionized calcium concentrations in animals with AP, including sequestration of calcium in peripancreatic fat as a result of saponification or in soft tissues, an increase in free fatty acid concentrations, an increase in calcitonin concentrations secondary to hyperglucagonemia, and parathyroid hormone resistance or deficiency secondary to hypomagnesemia. Further investigations are necessary to better characterize the underlying pathophysiologic abnormalities leading to low ionized calcium concentrations in cats with AP.

The overall fatality rate for cats with AP has not been reported previously; however, the fatality rate of 41% (19/46) in the present study appears to be better than the 80% rate reported for cats with concurrent AP and hepatic lipidosis. This difference may be attributable to the worse prognosis when concurrent disease occurs or to the more rapid or more frequent recognition of this disease in cats and improvements in treatment of affected cats since the previous study was reported.

Despite the absence of clinical signs associated with hypocalcemia in the present study, such as neurologic, electrolyte, or cardiac abnormalities, cats with AP in which ionized calcium concentration was low had a worse clinical outcome than did cats with AP in which ionized calcium concentration was within reference limits. In addition, ionized calcium concentrations were not significantly different between control cats that survived and control cats that did not survive, suggesting that hypocalcemia was associated with the severity of AP and not with some other factor in cats that did not survive. However, plasma ionized calcium concentration in cats with AP that survived was not significantly different from concentration in control cats, and previous studies have demonstrated an association between hypocalcemia and poor outcome not only for human patients with AP but also for critically ill adults and children with a variety of disease conditions. This may suggest that the poor outcome itself, rather than AP, was associated with hypocalcemia. Results of the present and previous studies cannot be used to determine whether the association...
between low ionized calcium concentration and poor clinical outcome represents a cause-and-effect relationship or is attributable to some other factor.

Although 12 of 27 (44%) cats with AP that survived had low plasma ionized calcium concentrations, only 3 had concentrations ≤ 1.00 mmol/L, whereas 10 of 19 (53%) cats that did not survive had plasma ionized calcium concentrations ≤ 1.00 mmol/L. Similarly, of the 13 cats with AP that had plasma ionized calcium concentrations ≤ 1.00 mmol/L, 10 (77%) did not survive. Therefore, although a plasma ionized calcium concentration > 1.00 mmol/L cannot be used to predict that a cat will survive, it may be appropriate to assign a worse prognosis or to institute more aggressive medical treatment in cats with AP that have plasma ionized calcium concentrations ≤ 1.00 mmol/L.

Plasma ionized calcium concentration was positively correlated with serum total calcium, total thyroxine, sodium, and albumin concentrations and negatively correlated with anion gap. However, all correlations were rather weak. This suggests that regulation of acid-base status and serum thyroxine, albumin, and electrolyte concentrations is multifactorial and unlikely to be greatly influenced by ionized calcium concentration. Likewise, regulation of ionized calcium concentration is multifactorial and unlikely to be greatly influenced by acid-base status or serum electrolyte or thyroxine concentrations. Alternatively, the variables assessed may not be directly related to ionized calcium concentration but, rather, to another process that results in corresponding changes in both variables. For example, malnutrition may result in both hypoalbuminemia, secondary to protein-calorie malnutrition, and hypocalcemia, secondary to vitamin and mineral deficiency. In addition, low thyroxine concentrations were more likely related to the "sick euthyroid syndrome" than a direct cause or effect of low ionized calcium concentration, and low thyroxine concentration likely serves as a marker of disease severity and clinical outcome, regardless of the particular disease process present.