Evaluation of serum values of pancreatic enzymes after endoscopic retrograde pancreatography in dogs

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Objective—To assess the safety of endoscopic retrograde pancreatography (ERP) in dogs by performing repeated clinical examinations and laboratory analyses of serum amylase, lipase, canine trypsin-like immunoreactivity (cTLI), and canine pancreatic elastase 1 (cE1) after the procedure.

Animals—7 healthy Beagles.

Procedures—Clinical examinations were performed and blood samples obtained for serum enzyme determinations before and at intervals (10 minutes; 2, 4, and 6 hours; and 1, 2, and 3 days) after ERP.

Results—Repeated clinical examinations revealed no signs of ERP-induced complications in the 7 dogs. Results of repeated laboratory tests indicated a transient increase in serum values of amylase, lipase, and cTLI but not cE1. Mean ± SD lipase activity increased from 120.7 ± 116.4 U/L to 243.4 ± 243.1 U/L at 4 hours after ERP. Median serum cTLI concentration increased from 16.2 µg/L (range, 7.7 to 26.5 µg/L) to 34.9 µg/L (range, 16.6 to 68.3 µg/L) 10 minutes after ERP. Enzyme values returned to baseline levels at the latest on day 2 in 6 of 7 dogs. Highest values for serum amylase, lipase, and cTLI and their delayed return to baseline values were detected in 1 dog with contrast filling of the pancreatic parenchyma.

Conclusions and Clinical Relevance—Results indicated that ERP appears to be a safe imaging technique of pancreatic ducts in healthy dogs, although it induced a transient increase in serum values of pancreatic enzymes. In dogs, repeated clinical examinations and serum enzyme determinations can be used to monitor ERP-induced complications such as acute pancreatitis. (Am J Vet Res 2004;65:616–619)

Endoscopic retrograde pancreatography (ERP) is an imaging technique of choice for the diagnosis and differentiation of chronic pancreatitis and pancreatic carcinoma in humans. Via this technique, it is also possible to detect different stages of chronic pancreatitis.1,3

In dogs, diagnosis of chronic pancreatitis and pancreatic carcinoma in a clinical setting is difficult because the signs and laboratory test results are nonspecific and routine imaging techniques are of limited diagnostic value.4 Data regarding the prevalence of chronic pancreatitis and pancreatic carcinoma in dogs are not available, although results of studies have indicated that both diseases are identified at necropsy as much as twice as frequently as pancreatic acinar atrophy.5,6 The use of ERP might improve clinical diagnosis of chronic pancreatic diseases in dogs. Other investigations7 have revealed that ERP is technically feasible in dogs and that pancreatograms produced via ERP correlate well with those obtained post-mortem.

Despite the apparently high diagnostic value of ERCP and ERP, use of this imaging technique can cause severe adverse effects in humans. Complication rates range from 0.7% to 1.38%2,9 for diagnostic ERCP performed in humans. In 1 study, observed complications included acute pancreatitis (0.2%), purulent cholangitis (0.16%), sepsis (0.12%), injury of the common bile duct (0.08%), misinterpretation of artifacts (0.08%), and sedative-induced adverse effects (0.08%). Sepsis or sedative-induced complications associated with ERCP were lethal in 0.04% of patients examined.2

The purpose of the study reported here was to assess the safety of ERP in healthy dogs by performing repeated clinical examinations and laboratory serum analyses of amylase, lipase, canine trypsin-like immunoreactivity (cTLI), and canine pancreatic elastase 1 (cE1) before and after ERP.

Materials and Methods

Dogs—Seven healthy Beagles (5 castrated males and 2 spayed females) without any history of gastrointestinal tract disorders were included in the study. Mean ± SD age of the dogs was 8.8 ± 1.2 years, and mean weight was 14.1 ± 3.0 kg. Prior to the study, all dogs were classified as clinically normal on the basis of findings of physical examination and results of assessments of full CBC and serum biochemical analyses. All procedures involving the dogs were approved by the Ethics Committee of the Veterinary Faculty, University of Helsinki, Finland.

Experimental design—Food was withheld from the dogs for 12 to 18 hours before and after the investigation. To perform ERP, dogs were premedicated with medetomidine and butorphanol and anesthesia was induced with propofol.
maintenance of anesthesia was achieved by inhalation of isoflurane with oxygen. In accordance with guidelines for the performance of ERCP in humans, dogs were administered enrofloxacin (5.0 mg/kg, IV) prior to ERCP. Each dog received a continuous IV infusion of physiologic saline (0.9% NaCl) solution during ERP, and dipyrone (metamizole; 40.0 to 50.0 mg/kg) was administered SC after the procedure.

For the ERP procedure, a standard ERCP catheter was inserted through the working channel of a side-view endoscope into the minor papilla of the duodenum. Via this catheter, the main pancreatic duct (duct of Santorini) was filled with an iodine contrast medium (iomeprol; 1.0 to 2.0 mL/dog) under fluoroscopic observation. Contrast administration was stopped when the main pancreatic ducts were clearly visible fluoroscopically.

Blood samples were collected from the dogs during repeated physical examinations before and 10 minutes, 2 hours, 4 hours, 6 hours, 1 day, 2 days, and 3 days after ERP. For each sample, the serum was separated from the blood clot immediately after clot formation and divided for analyses of 4 pancreatic enzymes. Samples for measurement of serum amylase and lipase activity were stored at 8°C for 4 to 12 hours until assessed with colorimetric assays. Serum samples for measurement of cTLI and cE1 concentrations were stored at −20°C until analyzed with species-specific immunoassays. The diagnostic accuracy of the cE1-ELISA was evaluated before analysis of the serum samples. The intra-assay variance was determined via measurement of cE1 concentration in 4 serum samples. The coefficient of variation was 11.6% for a cE1 concentration of 3.5 µg/L, 13.8% for 39.5 µg/L, and 4.4% for 80.9 µg/L.

Data analyses—Data for amylase and lipase were normally distributed and therefore described as mean ± SD and analyzed by use of a 1-way ANOVA for repeated measures over time. The Dunnett multiple comparison test was used to compare enzyme values after ERP with the baseline value. Serum cTLI and cE1 values were not normally distributed and therefore described as median, minimum, and maximum values and analyzed with the nonparametric ANOVA (Friedman test) followed by the Dunn post test. Values of \( P < 0.05 \) were considered significant. Statistical analyses were performed by use of a statistical software package.

Results

The ERP procedure was successfully performed on all 7 dogs with similar imaging results. The left and right parts of the duct of Santorini were filled with contrast medium through the minor papilla (Fig 1). In 1 dog (Beagle 1), an intramural injection of contrast medium close to the minor papilla was recorded. In another dog (Beagle 3), filling of the pancreatic parenchyma with contrast material occurred accidently.

Repeated physical examinations revealed no clinical abnormalities suggestive of ERP-induced complications in 6 of 7 dogs. One dog (Beagle 2) had slight signs of pain on palpation of the abdomen for 2 hours after ERP.

The determination of serum amylase activity before ERP revealed a mean baseline value of 695.3 ± 228.0 U/L (reference limit, < 1,200 U/L; Fig 2). After ERP, there was a transient increase in serum amylase activity; however, the change over time was not significant (\( P = 0.062 \)). The mean baseline activity of serum lipase was 120.7 ± 116.4 U/L (reference limit, < 90 U/L; Fig 3); before ERP, serum lipase activity was high in 2 dogs (Beagle 5, 368.9 U/L; Beagle 6, 166.7 U/L). After ERP, there was a transient increase in serum lipase activity; the change over time was significant (\( P < 0.001 \)). The median serum cTLI concentration before ERP was 16.2 µg/L (range, 7.7 to 26.5 µg/L; ref-
After ERP, serum cTLI concentration increased transiently; the change over time was significant \((P = 0.004)\). The median baseline serum cE1 concentration was 5.5 \(\mu g/L\) (range, 0.1 to 411.6 \(\mu g/L\)), and this value did not change significantly \((P = 0.446)\) after ERP (Fig 5). Reference values for serum cE1 concentration have not been established.

Serum amylase activity peaked \((1,152.4 \pm 425.0 U/L)\) 4 hours after ERP, but this value did not differ significantly from baseline value. Compared with baseline values, serum lipase activity was significantly increased at 4 hours \((423.4 \pm 243.1 U/L; P < 0.01)\) and 6 hours \((389.8 \pm 276.4 U/L; P < 0.05)\) after ERP. The highest serum cTLI concentrations were detected at 10 minutes (median, 34.9 \(\mu g/L\) [range, 16.6 to 68.3 \(\mu g/L\)]) and 2 hours (median, 32.3 \(\mu g/L\) [range, 16.5 to 52.2 \(\mu g/L\)]) after ERP. These values were significantly \((P < 0.05)\) higher than serum cTLI concentration on day 1 after ERP (median, 15.6 \(\mu g/L\) [range, 8.1 to 37.5 \(\mu g/L\)]) but were not significantly different from the baseline value.

High serum amylase activities and cTLI concentrations returned to baseline values on day 1 after ERP in 6 of 7 dogs and on day 2 after ERP in the remaining 1 dog (Beagle 3). Serum lipase activities returned to baseline values on day 1 after ERP in 2 dogs, day 2 after ERP in 4 dogs, and day 3 after ERP in 1 dog (Beagle 3). In the latter dog, the contrast filling of the pancreatic parenchyma also resulted in the highest serum amylase and lipase activities and cTLI concentration among the dogs during the entire study period (open triangle; Figs 2–4).

**Discussion**

In the healthy Beagles used in the study of this report, ERP did not cause clinically important complications such as acute pancreatitis. However, repeated determination of serum pancreatic enzyme values revealed transient increases in serum amylase, lipase, and cTLI values.

Similar transient increases in serum values of amylase, lipase, and TLI have been detected in humans after uncomplicated diagnostic ERP procedures. In dogs, a transient increase in serum pancreatic enzyme values without evidence of acute pancreatitis has been detected after manipulation of the pancreas, such as that which occurs during laparoscopic pancreatic biopsy procedures. All dogs included in our study were healthy; therefore, increases in serum pancreatic enzyme values that are associated with nonpancreatic causes, such as those resulting from renal failure, were excluded.

Thus, the observed transient increase in serum pancreatic enzyme values after ERP could be interpreted as a sign of reversible irritation of the exocrine pancreas by retrograde perfusion of an iodine contrast medium.

Unlike findings in humans, serum cE1 concentration in dogs did not parallel the time course of lipase and amylase activity after ERP. This difference might be explained by inclusion of patients with suspected pancreatic disease in the human studies, whereas the dogs of the study reported here were healthy.

Serum pancreatic enzyme values peaked at different times after ERP. Serum amylase and lipase activities reached peak levels at 4 and 6 hours after ERP, whereas serum cTLI concentration peaked earlier at 10 minutes and 2 hours after ERP. Similar time courses for changes in serum pancreatic enzyme values have been elucidated in humans after diagnostic ERP procedures. In an experimental model of edematous pancreatitis in dogs induced by hyperstimulation with cholecystokinin-8, serum cTLI concentration reached peak values and subsequently decreased sooner than serum amylase and lipase activities.

Serum amylase activity and cTLI concentration
returned to baseline values on day 1 in all but 1 dog (Beagle 3); similarly, serum lipase activity returned to baseline values on day 2 in all dogs except Beagle 3. Compared with findings in the other dogs, increases in the 3 serum pancreatic enzyme values detected in Beagle 3 were of the highest value and longest duration, probably as a result of filling of the pancreatic parenchyma with contrast medium. In humans, filling of the pancreatic parenchyma with contrast medium is a cause of ERP-induced acute pancreatitis.20,21 However, the level of serum lipase activity does not correlate with the degree of ERP-induced pancreatitis in humans.20,21 In human medicine, additional variables (eg, serum C-reactive protein and interleukin-6 concentrations) have been used to better assess the inflammatory response of the pancreas to ERP20,21; in this regard, the usefulness of measurement of serum C-reactive protein concentration after ERP in dogs remains to be investigated.20,21

Our findings indicated that ERP is a relatively safe diagnostic imaging technique in dogs. However, dogs undergoing ERP should be monitored by repeated physical examinations and pancreatic enzyme determinations performed on serum samples to identify potential ERP-induced complications, especially acute pancreatitis. Determination of serum amylase and lipase activities before ERP and on days 1 and 2 after the procedure appears to be sufficient for monitoring purposes in clinical practice. Amylase and lipase are the only pancreatic enzymes that can be routinely measured in serum within a short time. In dogs that develop acute pancreatitis, prolonged increases in amylase and lipase activities are to be expected.17–19 Measurement of serum cTLI concentration is of less value because this value decreases sooner in acute edematous pancreatitis than serum activities of amylase and lipase, despite ongoing inflammation.19 Moreover, serum cTLI concentration is determined with a radioimmunoassay that is generally performed at specialized laboratories, which delays acquisition of the test results. However, additional studies in dogs with suspected chronic pancreatic diseases would be required before monitoring guidelines for ERP procedures can be established.

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