Anything new in exocrine pancreatic insufficiency in dogs and cats

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Pathogenesis

Exocrine pancreatic insufficiency (EPI) is a syndrome caused by inadequate synthesis and secretion of pancreatic digestive enzymes. This subfunction of the exocrine pancreas leads to a maldigestion associated with diarrhoea and weight loss due to lack of enzymes, bicarbonate and other substances like intrinsic factor, antibacterial and trophic factors that are normally produced by the pancreas. The main causes of EPI are pancreatic acinar atrophy (PAA), chronic pancreatitis or potentially also hypo- or aplasia of the pancreas. However, neoplasia very rarely causes an EPI.

German Shepherds, rough-coated Collies, Chow Chows, Cavalier King Charles Spaniels and Corgis are predisposed, but EPI can be found in almost all breeds (1). Most cases of EPI in dogs are triggered by PAA. The aetiology of PAA is genetically determined and the predisposition to this disease appears to be inherited as an autosomal recessive trait. However, the exact genetic defect is unknown. The atrophy is most likely the result of an autoimmune disease, which leads to lymphocyte infiltration and subsequently to inflammation and atrophy (2). As in humans and cats, chronic pancreatitis is suggested to be the most common cause of EPI in Cavalier King Charles Spaniels. In this breed, the disease appears on average much later in life than in most other breeds (1). A few cases of EPI occur as a result of the obstruction of glandular outflow through an adenocarcinoma or as a complication following resection of the proximal small intestine. A congenital aplasia or hypoplasia of the pancreas may theoretically occur, but has not been proven in dogs or cats so far. Pancreatic flukes (Eurytrema procyonis) can also lead to EPI in endemic areas.

Clinical symptoms

It only comes to the formation of clinical symptoms when about 90 % of the functional capacity of the pancreas is lost. Since the pancreatic digestive enzymes occupy an important position in the assimilation of all dietary constituents, it is not surprising that malassimilation occurs in the absence of these enzymes. Parts of the food can no longer be decomposed sufficiently into smaller units and are therefore no longer available for absorption. The remaining food components in the intestinal lumen lead to the excretion of unformed faeces high in fat. The insufficient supply of the body can lead to weight loss, but also to vitamin deficiency symptoms. In cases where EPI is due to chronic pancreatitis, it may also lead to the secondary development of diabetes mellitus.

Diagnosis

Routine complete blood count and serum chemistry panel are in most cases without special findings. In a few cases, hyperglycaemia may occur due to diabetes mellitus with concomitant endocrine insufficiency.

The diagnosis is made in both the dog and the cat by the determination of trypsin-like immunoreactivity (TLI) in serum (3-5). For dogs, several tests are commercially available. The most commonly used test is a radioimmunoassay (RIA) with a reference range of 5-45 µg/l. It is important to note that EPI can only be diagnosed if TLI in serum is ≤ 2.5 µg/l. Patients with a serum TLI between 2.5 and 5 µg/l may well have an EPI, but in most cases, these animals suffer from chronic diseases of the small intestine (6). Therefore, in dogs with a value in this range a new cTLI determination should be performed after approximately 4 weeks. In addition, the patient should also be screened for possible small intestinal diseases. To the authors knowledge, for cats only one validated test for the determination of fTLI is available (Gastrointestinal Laboratory at Texas A & M University; www.cvm.tamu.edu/gilab). Therefore, most commercial labs send the serum to Texas.

Although PLI is a very reliable test for pancreatitis, it is clearly inferior to the determination of TLI for the diagnosis of EPI (mainly because of a greater overlap with healthy dogs; 7). More than a decade ago, a test to determine the elastase concentration in the canine faeces was evaluated (8). Since elastase is synthesized in the exocrine pancreas, elastase concentration in the faeces of dogs with EPI should be greatly reduced. This test showed acceptable sensitivity and specificity in this first study. However, the rate of true positive test results was only slightly above 50 %. A test to determine elastase concentration in faeces of cats is not available. Various other digestive tests, as well as the determination of faecal proteolytic activity, are offered by various laboratories. These tests are generally very variable and much less sensitive and specific than TLI. Therefore, these tests are at most indicated if one has no access to the much more reliable determination of TLI.

In patients with EPI, cobalamin and folic acid should also be determined in the serum. Most dogs (9) and cats (65 %; 3) with EPI have a cobalamin deficiency and should be treated accordingly. Recent studies have shown that cobalamin deficiency is a negative risk factor for dogs with EPI (9) and that cobalamin supplementation improved the response to treatment in cats (4). Secondary dysbiosis in the small intestine is also common in dogs with EPI.

Therapy

The supplementation with pancreatic extracts is the most important part in the treatment of dogs and cats with EPI. Dried commercial extracts from porcine or bovine pancreas are mostly used (e.g., Pancrex-Vet powder, Zoetis; Pancreatin, Albrecht). However, it is also possible to feed raw bovine, pork or wild animal pancreas (about 30 g per 10 kg of bodyweight (BW) with each meal). First, about one teaspoon of enzyme powder per 10 kg of BW should be added to each meal. An incubation of the food with the extract or a concomitant administration of bile salts is not necessary. Once a clinical improvement has occurred, an attempt can be made to reduce the amount of the given pancreatic extract. In some dogs, supplementation with raw pancreatic extract causes ulcers and bleeding of the oral mucosa. However, in most cases this will disappear again by reducing the dose. Most animals respond well to uncoated enzymes and enteric coating is not necessary. Furthermore, it is currently unknown if the more expensive enteric coated formulas are really superior (10) or not (11).

A reduction in the fat content in the nutrition is repeatedly discussed and recommended in animals with an EPI. However, this could lead to further malnutrition of the patient with fat-soluble vitamins and essential fatty acids. Only in a few cases a low-fat diet is necessary to achieve therapeutic success. In contrast, a reduction in the crude fibre content in the food seems to have a favourable effect, since crude fibres reduce the activity of the pancreatic enzymes.

As already mentioned, a large number of dogs and cats with EPI suffer from cobalamin deficiency. Accordingly, they should be treated with a pure cobalamin product since most vitamin combination preparations do not contain sufficiently high levels of cobalamin. Typically, the cobalamin is injected once a week for the first 6 weeks, then for 6 weeks every 2 weeks, and then once a month depending on the control results. The recommended dosages are between 250 µg (cats and dogs <5 kg), 400 µg (dogs 5-15 kg), 800 µg (dogs 15-30 kg), 1200 µg (30-45 kg) and 1500 µg for dogs > 45 kg. A new study has shown that at least in dogs with chronic diarrhoea, cobalamin can also be given orally (12). The recommended dosages are between ¼ (1-10 kg BW), ½ (10-20 kg BW) and 1 (> 20 kg BW) tablet containing 1 mg cyanocobalamin. However, since the intrinsic factor for the absorption of cobalamin in the ileum is produced only by the pancreas in cats (pancreas and stomach in dogs), cobalamin injection is safer with EPI.

Most patients favourably respond to enzyme and cobalamin supplementation. In cats or dogs, which do not respond to the therapy, the next attempt should be to diagnose and treat possible simultaneously occurring diseases of the gastrointestinal tract (e.g., food-responsive diarrhoea or IBD. Especially in cats, the number of cases with concurrent diseases seems to be high (58 %; 4). In cases with insufficient therapeutic success, dogs may be additionally treated for dysbiosis (e.g., metronidazole or tylosin for 1-4 weeks) or with antacids (e.g., proton pump inhibitors such as omeprazole). The lipase contained in the fed pancreatic extract is rapidly degraded by the low pH in the stomach. Increasing the pH in the stomach, however, in most cases does not promise to improve total fat digestion, as the pH change is likely to have a negative effect on the gastric lipase (and also on the protein degradation).

Prognosis

With appropriate therapy including cobalamin, most animals have a normal quality of life and a normal life expectancy. In one study, 19 % of dogs were euthanized in the first year, while the remaining dogs had an average life expectancy of more than 5 years (9).

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