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A Scoring Index for Disease Activity in Canine Inflammatory Bowel Disease

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The clinical course of inflammatory bowel disease (IBD) in dogs is characterized by spontaneous exacerbations and remissions, which makes assessment of disease burden difficult. The objectives of this study were to develop a scoring system for evaluation of canine IBD activity and to validate this scoring method by correlating it to objective laboratory and histologic indices of intestinal inflammation. Fifty-eight dogs with IBD were evaluated prospectively and compared to 9 disease-free control dogs. Clinical disease activity was quantified by a simple scoring system, the canine IBD activity index (CIBDAI), and compared to serum concentrations of C-reactive protein (CRP), haptoglobin (HAP), α-acid glycoprotein (AGP), and serum amyloid A (SAA), as well as histology scores derived from endoscopic biopsy specimens. Forty-six dogs were available for a reevaluation of the CIBDAI, CRP, HAP, and AGP, and 34 dogs had repeat analysis of SAA performed after medical therapy. Serum concentrations of CRP were significantly ($P < .02$) increased in dogs with CIBDAI scores ≥5 (mild disease activity or greater) compared to controls. Among IBD dogs, the CIBDAI showed good correlation ($r = 0.82$, $P < .0001$) to both histology and HAP scores, but CRP also was a strong co-correlate of disease activity. The IBD dogs showed significantly ($P < .0001$) decreased CIBDAI and CRP values but significantly ($P < .0001$) increased HAP concentrations after medical therapy compared to pretreatment values. We conclude that the CIBDAI is a reliable measure of inflammatory activity in canine IBD and that CRP is suitable for laboratory evaluation of the effect of therapy in these patients.

Key words: Acute-phase protein; C-reactive protein; Dog; Lymphocytic-plasmacytic enteritis.

Inflammatory bowel disease (IBD) in dogs is a chronic gastrointestinal tract disorder of unknown cause and ill-defined pathogenesis.[1,2] Clinical signs in dogs are highly variable, and the severity of disease may differ considerably among patients, depending on the localization and extent of affected regions of the gastrointestinal tract.[3–5] Furthermore, this diversity of signs impedes accurate evaluation of the effects of various therapies on inflammatory activity.[6,7] Thus, IBD in dogs is a highly individualistic disease, which makes assessment and comparison among patients difficult. A numeric index of the degree of illness (''activity'') is desirable because it serves to gauge initial IBD severity and guide therapeutic strategies.

Numerous clinical and laboratory indices of disease activity have been designed for use in human patients with IBD (Crohn disease and ulcerative colitis).[8–11] The most commonly used index is the Crohn disease activity index,[8] which emphasizes primarily clinical parameters, whereas other indices[10,11] incorporate objective laboratory variables of inflammatory activity. Increases in concentrations of serum proteins such as C-reactive protein (CRP) and orosomucoid (α_1-acid glycoprotein [AGP]) have been correlated with clinical disease activity in human patients with IBD.[12–18] Preliminary data obtained by a clinical scoring system, which reflects quantifiable and repeatable measures of disease activity in dogs with IBD, recently have been reported.[19]

An index of canine IBD activity would be helpful in the management of clinical patients, both as a measure of initial response to treatment and to assess long-term progress. This index also should prove useful in collaborative multicenter studies evaluating different forms of medical therapy. To this end, we have developed a simple and reliable scoring system for evaluating canine IBD activity and have attempted to validate its clinical application by correlating it to objective laboratory and histologic indices of intestinal inflammation.

Materials and Methods

Clinical Cases and Controls

Blood samples and tissue specimens were collected from 2 groups of dogs. The IBD group comprised 58 dogs diagnosed with IBD according to published criteria.[3,4] Briefly, criteria for selection included persistent (>3 weeks in duration) gastrointestinal signs, failure to respond to dietary (commercially prepared select antigen or highly digestible diets) or symptomatic therapies (paraciticides, antibiotics, anticholinergics, and gastrointestinal protectants) alone, failure to document other causes of gastroenteritis by thorough diagnostic evaluation, and histologic diagnosis of benign intestinal inflammation. The minimal diagnostic evaluation performed in all dogs with gastrointestinal signs included a CBC, serum biochemistry, urinalysis, direct smear and flotation examination of feces for nematode and protozoan parasites, and survey abdominal radiographs. In some instances, additional tests such as contrast radiography, abdominal ultrasonography, serum trypsinlike immunoreactivity, serum assays for folate and cobalamin, or some combination of these were performed as deemed appropriate by 2 of the authors (AEJ, CAS). Additionally, dogs that showed evidence of extra-alimentary tract inflammation (based on results obtained from initial diagnostic testing) or dogs that had received immunomodulatory drugs (eg, corticosteroids, metronidazole, and sulfasalazine) within 7 days before referral were excluded from further study.

The control group consisted of 9 adult, mixed-breed dogs of random

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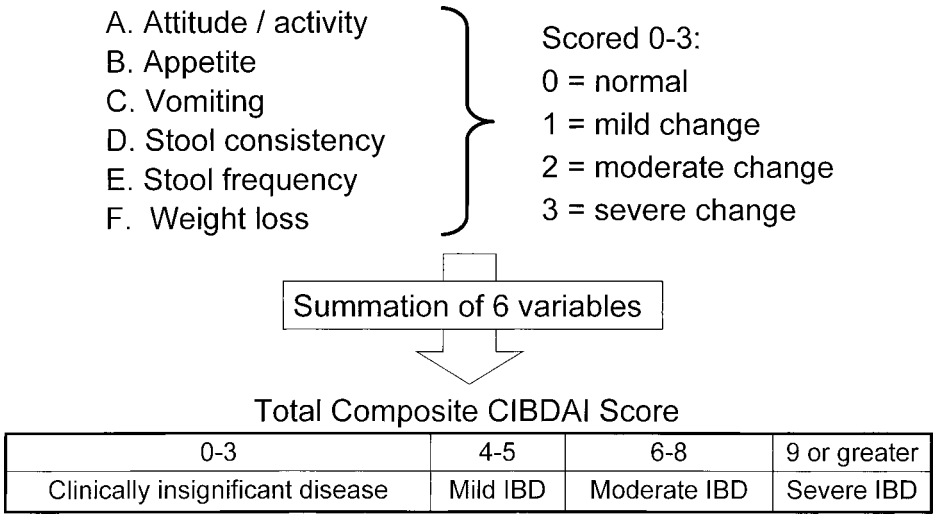

Fig 1. Criteria for assessment of the canine inflammatory bowel disease activity index (CIBDAI).

source origin that were free of gastrointestinal signs. Furthermore, control dogs were judged to be healthy on the basis of normal results on physical examination, CBC, serum biochemistry, urinalysis, multiple fecal examinations, and dirofilarial antigen assay.

Canine IBD Activity Index

Clinical disease activity was assessed by a simple numeric scoring system termed ''the canine IBD activity index'' (CIBDAI). Scoring criteria were modified in pilot studies until clinicians found an index that was repeatable and that correlated well among investigators. Under this system, 6 salient gastrointestinal signs were scored 0–3 by the gastroenterologist on the basis of the magnitude of their alteration from normal in a given IBD patient. Each parameter of the CIBDAI was assessed independently of the others as an average over time since the clinical signs had developed. Calculations of CIBDAI variables were as follows: (1) attitude/activity (0 = normal, 1 = slightly decreased, 2 = moderately decreased, and 3 = severely decreased); (2) appetite (0 = normal, 1 = slightly decreased, 2 = moderately decreased, and 3 = severely decreased); (3) vomiting (0 = none, 1 = mild [1 time/wk], 2 = moderate [2–3 times/wk], and 3 = severe [>3 times/wk]); (4) stool consistency (0 = normal, 1 = slightly soft feces or fecal blood, mucus, or both, 2 = very soft feces, and 3 = watery diarrhea); (5) stool frequency (0 = normal, 1 = slightly increased [2–3 times/d], 2 = moderately increased [4–5 times/d], and 3 = severely increased [>5 times/d]); and (6) weight loss (0 = none, 1 = mild [<5% loss], 2 = moderate [5–10% loss], and 3 = severe [>10% loss]). These scores then were summed, yielding a total cumulative CIBDAI score that reflected clinically insignificant disease or the presence of mild, moderate, or severe IBD (Fig 1).

Laboratory Analysis of Serum Acute-Phase Proteins

Serum acute-phase proteins (APPs) were measured by canine-specific commercial test kits or validated assays performed at research institutions.[20,a,b] The APPs evaluated included CRP, measured by enzyme-linked immunosorbent assay (ELISA) with canine CRP as a standard; haptoglobin (HAP), measured by a hemoglobin-HAP binding assay with bovine HAP as a standard; AGP, measured by radioimmunodiffusion with canine AGP as a standard; and serum amyloid A (SAA), measured by ELISA with canine SAA as a standard.

Histologic Examination of Endoscopically Obtained Biopsy Specimens

Multiple (10–15 per organ evaluated) mucosal biopsy specimens were obtained endoscopically from the stomach, small intestine, or large intestine of diseased dogs for microscopic review. Dogs having upper gastrointestinal signs (eg, vomiting, small bowel diarrhea, anorexia, and weight loss) underwent esophagogastroduodenoscopy, whereas dogs having only lower gastrointestinal signs (eg, tenesmus, hematochezia, mucoid feces, and frequent defecation) had a full colonoscopy performed to the cecum. Both upper and lower endoscopic examinations were performed in dogs having mixed signs of enterocolitis. Endoscopic lesions of increased granularity, increased friability, mucosal erosions, or some combination of these findings were observed in 52% of the IBD dogs. In these instances, multiple biopsy specimens were obtained directly from these lesions as well as from normal-appearing mucosa. Multiple biopsies from the gastric body, duodenum, or ascending, transverse, and descending colonic regions were obtained from all other dogs with IBD that had endoscopically normal mucosa. Mucosal specimens also were obtained from the stomach, small intestine, and colon of each control dog.

Histologic examination of all tissues was performed by a single pathologist (YN) who objectively graded endoscopic specimens and assigned a histologic lesion severity score for each dog. No information regarding history, clinical signs, or endoscopic observations was made available to the pathologist. A histologic grading system based on the extent of architectural disruption and mucosal epithelial changes was used.[3,6] In this scheme, mild IBD lesions were those with no mucosal disruption, glandular necrosis, immaturity (eg, delayed maturation or differentiation), or fibrosis of the lamina propria. Severe IBD was characterized by architectural distortion of the mucosa (extensive ulceration; necrosis; villus atrophy, fusion, or collapse; and glandular loss or severe glandular hyperplasia or fibrosis of the lamina propria). Moderate lesions were characterized by microscopic changes that varied in severity between these 2 extremes. No attempt was made to quantitate the number of inflammatory cells in the lamina propria of biopsy specimens. Rather, inflammatory cell types were included in the pathologist's report by means of standard classification schemes, including lymphocytic-plasmacytic, eosinophilic, suppurative, and granulomatous gastroenterocolitis based on the predominance of the cellular infiltrate.

Experimental Design and Data Collection

During an 18-month period (1999–2001), inflammatory activity (expressed as a numeric CIBDAI score) was evaluated prospectively in

Table 1. Pretreatment serum concentrations of acute-phase proteins in healthy dogs and dogs with inflammatory bowel disease.[a]

Group	AGP (μg/mL)	CRP (μg/mL)	HAP (mg/mL)	SAA[b] (ng/mL)
Healthy dogs (n = 9)	261.1 ± 110.5	1.53 ± 0.55	3.20 ± 0.79	124.5** ± 27.4
IBD dogs (n = 58)	363.4 ± 44.2	10.42* ± 2.56	2.50 ± 0.37	14.1 ± 6.2

AGP, α-acid glycoprotein; CRP, C-reactive protein; HAP, haptoglobin; SAA, serum amyloid A; IBD, inflammatory bowel disease.

[a] Data are expressed as mean plus or minus standard error of the mean.

[b] Assays performed in 7 healthy dogs and in 36 dogs with IBD.

* $P < .07$ compared to healthy dogs; ** $P < .0001$ compared to IBD dogs.

58 dogs with IBD and 9 control dogs without clinically apparent gastrointestinal disease by 2 primary investigators (AEJ or CAS). Controls[19] were monitored closely on a daily basis and remained free of gastrointestinal signs for >90 days. Initial CIBDAI scores were recorded for each dog before endoscopy. Concurrent with endoscopic examination, serum was collected, divided into 200- to 500-μL aliquots, and stored at −70°C for later analysis. Baseline (pretreatment) AGP, CRP, and HAP were measured in all 58 IBD dogs and in the 9 control dogs. Pretreatment SAA was measured in 36 IBD dogs and 7 control dogs. Insufficient serum volume precluded duplicate analysis of SAA in the other control and IBD dogs. To establish whether medical therapy influenced inflammatory activity, both the CIBDAI and serum APPs were reevaluated in most of the IBD dogs after 14–21 days of medical therapy. Posttreatment measurement of AGP, CRP, and HAP was performed in 46 dogs. The owners of 9 of the IBD dogs for which initial APP analysis was performed failed to return for subsequent posttreatment APP measurement. Additionally, 3 of these 9 dogs that had only baseline APPs determined were euthanized or died, presumably as a consequence of their severe gastrointestinal disease. Furthermore, serum from 2 of the 3 deceased IBD dogs was not available for posttreatment measurement of SAA.

Statistical Analysis

All data are expressed as the mean plus or minus the standard error of the mean. Nonparametric Wilcoxon rank sum tests were used to assess group differences, either IBD versus control or pre- and posttreatment. Wilcoxon rank sum tests also were used to assess the significance of the organs involved (eg, gastritis, enteritis, and colitis) on changes in serum APPs for most IBD dogs. A P value <.05 was considered significant. Stepwise multiple regression analysis determined the best fit regression equation (eg, optimal combination of variables) for prediction of the actual CIBDAI.

Results

The IBD group included 31 males and 27 females. The affected dogs were middle-aged, with a mean age at presentation of 6.1 years (range, 1–13 years). All dogs had histories of chronic gastrointestinal signs (mean duration, 5.4 months; range, 1.5–40 months) that were best characterized as cyclic. In this regard, dogs would exhibit overt gastrointestinal signs for several days, after which time these signs would resolve spontaneously and recur at a later date. Disease location, based on histologic lesions present in biopsy specimens, was stomach alone in 5 dogs, stomach and small intestine in 7 dogs, small intestine alone in 25 dogs, and colon alone in 7 dogs; 14 dogs had enterocolitis. A review of histologic severity scores revealed that 61% of the dogs had moderate-to-severe histologic lesions, whereas the remaining 39% of dogs had less severe histologic findings. The cellular infiltrate in all mucosal specimens was predominantly lymphocytes and plasma cells, usually accompanied by an admixture of eosinophils, neutrophils, macrophages, or some combination of these cell types. No dogs were noted to have a predominant eosinophilic infiltrate, but higher than expected numbers of eosinophils were observed in intestinal tissues from 4 dogs.

All IBD dogs were evaluated together as a single group for comparison to the group of healthy control dogs because statistical analysis failed to detect differences in serum APPs with regard to the organ of involvement. Table 1 shows the comparison of serum APPs at the time of endoscopy in the 2 dog groups. Concentrations of SAA were significantly ($P < .001$) higher in healthy dogs than in dogs with IBD. In IBD dogs, high concentrations of both CRP and AGP were apparent, with increased CRP concentrations approaching significance ($P < .07$) for diseased dogs compared to control dogs. However, when evaluating IBD dogs having CIBDAI scores of at least 5 (ie, mild disease activity or greater), significantly ($P < .02$) increased CRP concentrations were observed compared to healthy controls (Table 2). Multiple regression analysis was used to determine which combination of variables best predicted the CIBDAI. The best correlation ($r = 0.82$, $P < .001$) was observed when the HAP and histologic scores were compared (Fig 2).

Marked alterations in CIBDAI scores and CRP and HAP concentrations were observed after medical management of IBD (Table 3). All IBD dogs were managed with dietary therapy and immunomodulatory drugs to reduce gastrointestinal inflammation. Dogs were fed one of several commercially available enteric diets having more than one of the following characteristics: minimal residue and high di-

Table 2. Concentrations of CRP in healthy dogs and in IBD dogs having CIBDAI scores ≥5.[a]

Group	CRP (μg/mL)
Healthy dogs (n = 9)	1.53 ± 0.55
IBD dogs (n = 28)	15.33 ± 4.85*

CRP, C-reactive protein; CIBDAI, canine inflammatory bowel disease activity index; IBD, inflammatory bowel disease.

[a] Data are expressed as mean plus or minus standard error of the mean.

* $P < .02$ compared to healthy dogs.

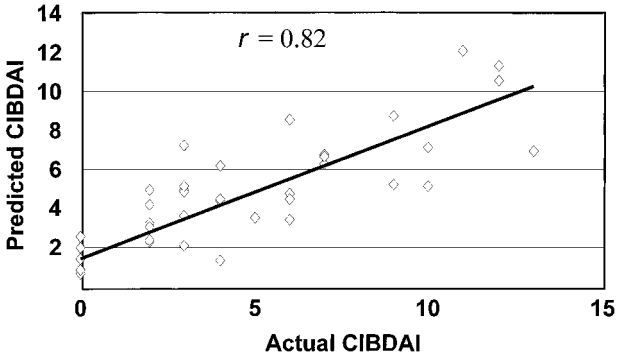

Fig 2. Correlation between the predicted canine inflammatory bowel disease activity index (CIBDAI) and the actual CIBDAI in dogs with inflammatory bowel disease. y = histology score (HISTO) + HISTO^2 + log haptoglobin (HAP) + HAP^3 + HAP.

gestibility, selected protein (limited antigen) source, protein hydrolysates, or some combination of these features. All other dietary treats and supplements were avoided if at all possible. The majority (>85%) of dogs received a standard combination of drugs consisting of prednisone (0.5–1.5 mg/kg PO q12h) and metronidazole (5–10 mg/kg PO q12h) during the treatment period. Combination drug therapy was used to minimize adverse effects of glucocorticoids such as polyuria, polydipsia, and excessive panting. Two dogs with moderately severe lymphocytic-plasmacytic gastroenteritis also were treated with a histamine-2 receptor antagonist (ranitidine 2 mg/kg PO q12h). Three dogs with colitis were treated with sulfasalazine (25 mg/kg PO q12h) alone, and all dogs with large bowel signs or histologic evidence of colitis received moderately insoluble fiber supplementation (0.25–0.5 teaspoon or tablespoon per meal, depending on body weight).

Reexamination of all IBD dogs with assignment of posttreatment CIBDAI scores was performed by a study gastroenterologist (AEJ or CAS). Whenever possible, the same clinician who performed the initial patient evaluation performed the recheck evaluation. Repeat CIBDAI scores were derived after patient examination and client interview. Each variable was rescored in comparison to its pretreatment value. For example, if there was no change in a given CIBDAI parameter, it was assigned the same score during the posttreatment period that it had received during the pretreatment period. If the severity of a parameter worsened, the severity score was increased to the next greater value than was recorded previously. Conversely, if a CIBDAI parameter decreased in clinical severity, the severity score for this parameter was decreased to the next lower value compared to its pretreatment value. These 6 variables again were summed, yielding the final composite posttreatment CIBDAI score for each dog.

HAP significantly ($P < .0001$) increased, whereas both the CRP and CIBDAI significantly ($P < .0001$) decreased during the 14- to 21-day posttreatment period compared to their pretreatment values. Owner perception of and satisfaction with clinical improvement generally paralleled alterations in CIBDAI scores during the treatment period. In this regard, the majority (82%) of dogs that improved clinically (as reported by the client) also had reductions in their CIBDAI scores after therapy. Conversely, dogs that failed to respond to initial medical therapy, as reported by their owners, also tended to have posttreatment CIBDAI scores that varied little from pretreatment values.

Table 3. The effects of therapy on canine IBD indices.[a]

Variable	Pretreatment	Posttreatment	*P*-Value
CIBDAI	5.5 ± 0.4	1.6 ± 0.3	.0001
SAA[b]	14.1 ± 6.2	4.7 ± 0.8	.5130
HAP	2.5 ± 0.4	9.5 ± 1.1	.0001
CRP	10.4 ± 2.5	0.6 ± 0.1	.0001
AGP	363.4 ± 44.2	355.0 ± 52.1	.8727

IBD, inflammatory bowl disease; CIBDAI, canine IBD activity index; SAA, serum amyloid A; HAP, haptoglobin; CRP, C-reactive protein; AGP, acid glycoprotein.

[a] Data are expressed as mean plus or minus standard error of the mean.

[b] Pretreatment assays performed in 36 dogs and posttreatment assays performed in 34 dogs.

Discussion

The assessment of clinical severity (activity) in dogs with IBD is difficult. The clinical condition at a particular time may be influenced by the presence of active intestinal inflammation as well as secondary consequences of inflammation, including anemia and vitamin deficiencies that contribute to the diverse signs of gastrointestinal disease. The definition of disease activity used in the present study was patterned after those used in humans with IBD.[8–10,12,21] Specifically, we used the frequency and severity of clinical signs such as vomiting and diarrhea as clinical consequences of diffuse mucosal inflammation. The selection of variables comprising the CIBDAI was based on prospective pilot studies,[19] critical review of previous cases of canine IBD diagnosed at our institution, previous experiences with IBD in dogs,[3,6,7,22–26] and case-based or clinical research studies reported by others.[1,2,4,5,27–30] Nevertheless, some ambiguity in the CIBDAI scoring criteria may occur. For example, dogs will not necessarily be rated as severe in all 6 criteria, which is one reason for considering supplementary approaches (such as measurement of serum CRP concentration) to categorize and assess disease activity in canine IBD. These same limitations may apply to indices of IBD in humans.[8–10,12,21]

No published reports quantitatively define the severity of clinical signs in dogs with IBD. Presently, clinical staging depends primarily on subjective patient assessment and is further hampered by poorly standardized histologic grading schemes and personal experiences.[6,31–33] Our proposed index is the 1st attempt to develop a simple yet practical scoring system for assessment of the dynamic changes that reflect the course of IBD in dogs. These data indicate that the CIBDAI is a useful method for assessing clinical disease activity in dogs with IBD at diagnosis. Furthermore, changes in the CIBDAI were accompanied by alterations in APP concentrations during treatment, suggesting that medical management may alter APP concentrations.

Clinical indices remain the most widely used tools in assessing disease activity in humans with IBD, either in

practice or in clinical trials.[21] The Crohn disease activity index uses 8 variables to enumerate ''global'' IBD clinical status,[8] whereas others[9] have proposed a simpler Crohn scoring system that reflects subtle daily variations in gastrointestinal health. The Truelove and Witts definition of ulcerative colitis provides 2 easily measurable clinical parameters (frequency of defecation and extent of macroscopic blood loss) for determination of disease activity.[10] Others have suggested use of a combination of clinical (eg, body weight and stool consistency) and laboratory (eg, serum albumin concentration, erythrocyte sedimentation rate, and serum APP concentrations) markers to more objectively quantitate intestinal inflammatory activity.[10,11]

Various indices have been used to assess IBD activity in dogs, including clinical signs,[3,4] histologic grades of mucosal inflammation,[3,5,27,31] phenotypic analysis of immune cells,[22,23,28,29,34] measurement of inflammatory mediators such as metabolites of nitric oxide,[24,25] and altered expression of cytokine messenger RNA transcripts.[26,30] Although potentially useful in a research setting, the application of most of these variables in daily clinical practice is cumbersome and technically challenging. We chose to develop a simplified scoring index based on 6 key gastrointestinal signs thought to be important indicators of disease activity. Additionally, the CIBDAI provides a number of features considered useful in the evaluation of humans with IBD, including the following: (1) it incorporates major gastrointestinal signs; (2) it uses observations that are apparent in a clinical setting; (3) it incorporates visit-to-visit changes in disease activity; (4) it is easily calculated; (5) it correlates with objective indices of disease activity; and (6) it provides prognostic information about disease activity before and after therapy.[8]

A major goal of this study was to correlate the CIBDAI to objective parameters of intestinal inflammation. Given the limitations of histologic interpretation of biopsy specimens (eg, absence of uniform and objective grading criteria for diagnosis of canine IBD[6,31,32]) and the inability to repeat the intestinal biopsy after therapy in most dogs, we evaluated the measurement of serum APP concentrations as supportive laboratory markers of inflammation. APPs are plasma proteins produced by the liver that increase dramatically during acute inflammation.[35] Studies in several species have identified interleukin-1, tumor necrosis factor α, and interleukin-6 as the prime inducers of hepatic APP synthesis.[36,37] APPs assume a variety of roles in inflammation, including participation in host defense, protease inhibition, and scavenging of reactive oxygen species.[38] Serum concentrations of APPs have been shown to be useful indicators of disease activity in humans with cancer, bacterial infection, and connective tissue disorders such as rheumatoid arthritis.[39–41] The magnitude of the APP response is approximately proportional to the activity or mass of inflamed tissue during acute inflammation. Surgical trauma, fractures, lacerations, and experimental endocarditis and gastritis result in increased serum concentrations of several acute-phase reactants in dogs, especially CRP.[20,42,43]

The role of APPs as laboratory markers in human patients with IBD has been investigated extensively. In most studies, both CRP and AGP correlate well with other assessments, including endoscopic appearance, disease extent, and fecal leukocyte excretion.[14,16–18] Concentrations of SAA usually are higher in Crohn disease than in ulcerative colitis.[44] Others report that CRP, AGP, and α_1-antitrypsin vary with disease activity and have discriminating value in differentiating active from quiescent IBD.[45] The analysis of APPs in the IBD dogs of the present study was based on their proven utility as laboratory markers in human patients with IBD and pilot studies of IBD in dogs as well as the availability of canine-specific assays for their measurement.

The observation of increased pretreatment SAA concentrations in control animals that were thought to be free of pathologic (eg, inflammatory) conditions was surprising and cannot be completely explained. However, these dogs were not family pets and were not accustomed to restraint for examination and blood sampling. It is possible that stress associated with these procedures caused increased endogenous cortisol secretion, resulting in increased concentrations of SAA in these animals.[46] A study in calves has shown that physical stress increases SAA concentrations.[47]

The goal of the present study was to develop a useful clinical index that could assess the spectrum (ie, mild to severe) of disease activity characteristic of canine IBD. Mean concentrations of CRP and AGP were increased in the IBD group at the time of diagnosis, with dramatic increases in CRP observed in 28 IBD dogs with CIBDAI scores $\geq$5. This finding was not unexpected, and it likely reflected differences in disease activity (ie, active versus quiescent) at presentation. Indeed, the highest CIBDAI scores were observed in those dogs having overt gastrointestinal signs such as weight loss, vomiting, diarrhea, melena, and tenesmus. Changes in other serum APP concentrations, however, did not parallel changes in the CIBDAI as well as did changes in CRP. Nevertheless, our findings indicate that CRP is a useful laboratory marker of inflammatory activity in IBD dogs with clinically significant disease as indicated by a CIBDAI score of at least 5.

A similar trend of increasing AGP associated with increased CIBDAI scores also was observed, but this association became significant only when CIBDAI scores were $\geq$6. HAP did not achieve significance as a serologic marker of disease activity in IBD dogs before therapy. This finding was unexpected because both HAP and histology scores were highly correlated with the CIBDAI. The substitution of CRP for HAP in the regression equation resulted in a virtually identical r value of 0.82 but a slightly reduced adjusted r^2 value. Therefore, HAP was chosen as the other variable in derivation of the final CIBDAI regression equation, although CRP also was a very strong co-correlate of disease activity.

To explore the prognostic usefulness of the CIBDAI, we compared the pretreatment CIBDAI scores and serum APP concentrations in 46 IBD dogs to their posttreatment values. Reevaluations were performed after 14–21 days of medical therapy consisting of dietary trials and immunomodulatory drugs (glucocorticoids, metronidazole, and sulfasalazine). This time frame for the reevaluation of dogs with IBD is standard practice at our institution and generally is adequate to assess response to medical therapy. Additionally, this interval encouraged client compliance. The mean CIBDAI decreased markedly in treated dogs from 5.5 to 1.6 and was accompanied by a dramatically decreased CRP concentra-

tion (from 10.4 to 0.6 μg/mL). A control group of untreated diseased dogs would be required to more completely assess the effect of treatment. However, use of the treated diseased dogs as their own controls shows the ability of the index to measure the efficacy of treatment.

Improvement in CIBDAI scores during the posttreatment period could have occurred because of natural disease fluctuation rather than response to medical therapy. We observed very good to excellent control of gastrointestinal signs in most IBD dogs during the 2- to 3-week treatment period. However, additional studies evaluating disease severity over a longer follow-up period would be required to conclusively differentiate initial response to therapy from spontaneous fluctuations in disease activity.

In addition to CRP, the mean HAP concentration in treated dogs was increased compared to pretreatment concentrations. Glucocorticoid therapy could have contributed to increases in serum HAP in some dogs.[48,49] Steroid-induced increases in serum HAP also have been recognized in sheep.[50] The mechanism by which HAP concentrations increase in dogs after exogenous glucocorticoid administration remains unknown, but it is unlikely that stress-related endogenous cortisol secretion contributes substantially to this phenomenon.[49] Nevertheless, the concordance of the CIBDAI and CRP in treated dogs in the present study suggests that these parameters provide important prognostic information for monitoring therapeutic response during the induction phase of therapy.

We also evaluated APPs in 14 dogs with a variety of non-IBD enteric and extra-alimentary tract inflammatory diseases. As a group, these dogs had markedly increased serum CRP, SAA, and AGP concentrations compared to IBD dogs (data not shown). These preliminary data suggest that non-IBD dogs with other inflammatory disorders have different APP profiles, perhaps as a consequence of more severe localized inflammation, which induces greater hepatic APP synthesis.[35–40]

In conclusion, our findings indicate that the CIBDAI is a reliable measure of clinical signs of inflammation in dogs with IBD. Both the CIBDAI and the CRP decrease in successfully treated dogs, suggesting that CRP is suitable for laboratory evaluation of the effect of therapy in these patients. One important caveat that must be emphasized is that altered CRP is not specific for gastrointestinal inflammation. Other concurrent infections or inflammatory conditions that cause an acute-phase response also must be considered.[51]

Footnotes

[a] Canine-specific validated assays, Clinical Biochemistry Section, Department of Veterinary Clinical Sciences, Glasgow University Veterinary School, Glasgow, Scotland

[b] Canine-specific commercial test kits, Tri-Delta Diagnostics, Morris Plains, NJ

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