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Research article / Научная статья

Pathogenetic factors associated with formation of acute abdominal pain syndrome in dogs with gastroenteritis

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Abstract. Intercorrelative relationships between various clinical and laboratory parameters in dogs with acute gastroenteritis were studied. In dogs with acute alimentary gastroenteritis (n=31), pain rating scale score significantly ($p \le 0.05$) correlated with pulse rate (r = 0.58), respiratory rate (r = 0.50), hematocrit (r = 0.47), ESR (r = 0.72), number of erythrocytes (r = 0.50) and leukocytes (r = 0.77), concentration of albumins (r = -0.52), globulins (r = 0.59), α 1-globulins (r = 0.49), α 2-globulins (r=0.42), β -globulins (r=-0.36), γ -globulins (r=0.59), C-reactive protein (r= 0.82), serum activity of ALT (r=0.70), AST (r=0.39), α -amylase (r=0.38), alkaline phosphatase (r = 0.83) and serum concentration of creatinine (r = 0.42), tumor necrosis factor- α (r = 0.82), interleukin-4 (r = 0.92), interleukin-6 (r = 0.92), interferon- γ (r=0.91), interleukin-1 α (r = 0.85), interleukin-8 (r = 0.91). The following changes were noted in the body of dogs with acute gastroenteritis: local and systemic immune-inflammatory response activated, pain, intoxication, dehydration syndrome, disorders of motor, secretory, absorption, excretory function of gastrointestinal tract formed, secondary hepatopathy and pancreatopathy developed. In dogs with acute gastroenteritis, there were also statistically significant ($p \le 0.05$) correlations between the number of erythrocytes and hematocrit (r = 0.65), MCHC (r = 0.32), ESR (r = 0.35), hemoglobin concentration (r = 0.73) and leukocyte count (r = 0.35); between MCV and hematocrit (r = 0.62), MCHC (r = -0.64); between MCV and MCHC (r = -0.64); MCH and MCHC (r = 0.40); ESR and leukocyte count (r = 0.53). Changes in intercorrelative relationships between clinical and laboratory parameters in dogs with acute gastroenteritis can be considered as predictors of severity of the pathological process.

Key words: acute gastroenteritis, pain, pathogenesis, correlation, inflammation, immunology, hematology

Conflicts of interest. The authors declared no conflicts of interest.

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Introduction

Acute alimentary inflammatory diseases of gastrointestinal tract in animals of all species remain an urgent problem in veterinary medicine due to their wide prevalence, high probability of a severe course and possibility of lethal outcome, especially in young animals [1–4].

Every year, about 1 million cases of acute diseases in dogs are registered in the Russian Federation, accompanied by diarrhea, vomiting, hypovolemia, intoxication, and dysfunction of many body systems [5, 6]. It should also be noted that the actual incidence of gastroenteritis in animals can be much higher than official statistics due to mild forms of pathology, treatment of which is carried out by pet owners at home [7–10]. Gastroenteritis in dogs is accompanied by alterative and inflammatory changes in the wall of gastrointestinal tract, often complicated by pain, intoxication, dehydration, hypovolemia, systemic changes in body, disorders of motor, secretory, protective, absorption and excretory functions of intestine and stomach [1, 11]. Activation of opportunistic bacteria and malignant changes in qualitative and quantitative characteristics of intestinal microbiome contribute to progression of gastrointestinal diseases in animals [12–16]. Many aspects of the mechanisms of development and progression, as well as sanogenetic characteristics in dogs with acute gastroenteritis, remain poorly understood. Therefore, clinical and experimental substantiations of pathogenetic factors in gastroenteritis in dogs are relevant, and their elimination will reduce the frequency of hospitalization and improve therapeutic efficacy.

The aim of the study was to identify and analyze pathogenetic correlations between clinical and laboratory parameters in dogs with gastroenteritis complicated by abdominal pain.

Materials and methods

Clinical, instrumental and laboratory studies were carried out in the veterinary center 'Vetmaster' (Ramenskoye, Moscow region). The objects of the study were dogs of dwarf and small breeds with acute gastroenteritis, aged 2–5 years, which came to the veterinary center.

Selection of sick animals was carried out by an integrated approach using inclusion and exclusion criteria [17, 18]. The inclusion criteria for dogs with gastroenteritis in the study were the presence of clinical and laboratory, ultrasonographic, radiographic signs of acute inflammatory process in gastrointestinal tract. Exclusion criteria — other types of gastroenteritis, parasitic, infectious diseases (coronavirus and parvovirus enteritis, carnivore distemper), food allergy, malabsorption syndrome, neoplasia or foreign bodies of gastrointestinal tract.

Diagnostic search for acute gastroenteritis in dogs was performed in a complex manner, considering the analysis of anamnesis data, clinical diagnostics, morphological and biochemical

blood tests, radiography (EcoRay Orange-1060HF device, Korea) and sonography (Mindray DC-90 Vet device, China) [15, 16]. Physical examination of sick dogs was performed according to the standard method [18, 19]. A four-point visual scale for assessing severity of pain syndrome from Colorado State University (CSU) was used [9, 11].

Based on inclusion and exclusion criteria, 31 dogs with gastroenteritis were included in the study. The control group included 15 physiologically healthy dogs of dwarf and small breeds, aged 2–5 years.

Clinical blood analysis was performed according to a unified method on URIT-2900 Vet Plus analyzer (China) [20, 21]. The following hematological parameters were assessed: hemoglobin, erythrocytes, leukocytes, hematocrit, mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular volume (MCV). The erythrocyte sedimentation rate (ESR) was measured by the Panchenkov method [12, 16]. Biochemical parameters of blood serum were studied on a URIT-880 Vet (China) using standard sets of consumables. Fractional analysis (proteinograms) of blood serum, as well as concentration of β -lipoproteins, were analyzed by the turbidimetric method using FEK-56PM (Russia) [3, 8]. Level of C-reactive protein was assessed using a latex diagnosticum (CRP-latex test) [22]. Serum bilirubin concentration was measured by colorimetric method. Concentration of cytokines in blood serum was assessed on a Multiskan FC photometer (Shanghai) with a built-in shaker for 96 wells using a spectral range of 450 nm and test systems for enzyme immunoassay (interferon- γ , interleukin-1 α , interleukin-6, interleukin-8, ('Tsitokin', Russia) [10].

Statistical processing of primary experimental digital data was carried out on a personal computer (AMD Athlon 3000G with Radeon Vega Graphics 3.5 GHz, RAM 8.00 GB) using statistical program Statistica 7.0 (USA). The assessment of normality of distribution of signs was assessed by the Shapiro-Wilk test [21]. The presence of correlations was checked using the nonparametric Spearman test. Statistical significance was considered sufficient at $p \le 0.05$ [22].

Results and Discussion

Using the method of nonparametric correlation analysis (Spearman's test), a matrix of intercorrelations was constructed regarding clinical parameters in dogs with acute gastroenteritis, depending on the presence of complication in form of abdominal pain syndrome (Table 1).

Table 1

Intercorrelation matrix (r) of clinical parameters in dogs with gastroenteritis depending on presence of acute abdominal pain syndrome

Index	Pain Rating Scale	Temperature	Pulse	Respiratory rate
Pain Rating Scale	1.00	0.28	0.54*	0.50*
Temperature	0.28	1.00	0.43*	0.16
Pulse	0.54*	0.43*	1.00	0.27
Respiratory rate	0.50*	0.16	0.27	1.00

Note: * - correlation dependence is significant (p \leq 0.05; Spearman's test).

Table 1 shows that in dogs with acute gastroenteritis, pain rating scale score significantly correlated with pulse rate (r = 0.58; $p \le 0.05$) and respiratory rate (r = 0.50; $p \le 0.05$), and body temperature was statistically significantly correlated with pulse rate (r = 0.43; $p \le 0.05$). In the mechanisms of development and progression of acute gastroenteritis in dogs, mucous membrane of gastrointestinal tract is irritated by feed components, which causes changes in its motor and secretory function [3, 7]. Subsequently, neuroendocrine system activates, activity of local hormonal and peptide regulation of stomach and intestines changes, which lead to pathological changes in enterogastric, enterocholikinetic, enterohepatic and enteropancreatic systems [11, 18]. All these changes have a stimulating effect on growth and development of opportunistic intestinal microflora [14]. In turn, lipopolysaccharides of microbial cell membrane, in particular flagellin, exo- and endotoxins, irritate and cause secondary alterative changes in mucosa and other tissues of the stomach and intestine wall, which lead to manifestation and progression of acute gastroenteritis in sick dogs [1, 7, 15].

A comparative analysis of matrix of intercorrelations of general clinical blood parameters in dogs with acute gastroenteritis depending on the presence of abdominal pain syndrome was carried out (Table 2).

Table 2

Index	Pain Rating Scale	Hematocrit	Erythrocytes	Hemoglobin	MCV	MCH	MCHC	ESR	Leukocytes
Pain Rating Scale	1.00	0.47*	0.50*	0.27	0.10	-0.15	-0.10	0.72*	0.77*
Hematocrit	0.47*	1.00	0.65*	0.65*	0.62*	0.21	-0.19	0.38*	0.34*
Erythrocytes	0.50*	0.65*	1.00	0.73*	-0.15	-0.05	0.32*	0.35*	0.35*
Hemoglobin	0.27	0.65*	0.73*	1.00	0.07	0.62*	0.53*	0.33*	0.15
MCV	0.10	0.62*	-0.15	0.07	1.00	0.26	-0.64*	0.15	0.09
МСН	-0.15	0.21	-0.05	0.62*	0.26	1.00	0.40*	0.13	-0.18
МСНС	-0.10	-0.19	0.32*	0.53*	-0.64*	0.40*	1.00	0.05	-0.14
ESR	0.72*	0.38*	0.35*	0.33*	0.15	0.13	0.05	1.00	0.53*
Leukocytes	0.77*	0.34*	0.35*	0.15	0.09	-0.18	-0.14	0.53*	1.00

Matrix of intercorrelations (r) of general clinical blood parameters in dogs with gastroenteritis depending on presence of acute abdominal pain syndrome

Note: * – correlation dependence is significant ($p \le 0.05$; Spearman's test).

It was found that in the body of dogs with acute gastroenteritis (see Table 2), in the pathogenesis of development of general pathological changes, statistically significant correlations were formed between pain rating scale and hematocrit, number of erythrocytes and leukocytes. It was also stated that there were statistically significant correlations between number of erythrocytes and hematocrit, MCHC, ESR, hemoglobin concentration and the number of leukocytes; between MCV and hematocrit, MCHC; between MCV and MCHC; MCH and MCHC; ESR and leukocyte count. In acute gastroenteritis, dogs develop a systemic inflammatory response, which manifests itself as neutrophilic leukocytosis and accelerated ESR [5, 9]. When the primary disease was complicated by pain syndrome, degree of neutrophilia was significantly higher [1, 4]. At the same time, against the background of a systemic inflammatory reaction, rheological changes in blood composition and dysproteinemia develop in dogs with gastroenteritis, which cause an increase in ESR [10].

Analysis of dependence of intercorrelations between biochemical parameters of blood serum characterizing protein metabolism in dogs with gastroenteritis and the presence of acute abdominal pain syndrome is given in Table 3.

Table 3

Index	Pain Rating Scale	Total protein	Albumins	Globulins	a1-globulins	a2-globulins	ß-globulins	y-globulins	C-reactive protein
Pain Rating Scale	1.00	0.21	-0.52*	0.59*	0.49*	0.42*	-0.36*	0.59*	0.82*
Total protein	0.21	1.00	0.15	0.68*	0.13	0.18	0.38*	0.47*	0.20
Albumins	-0.52*	0.15	1.00	-0.57*	-0.44*	-0.36*	0.22	-0.35*	-0.41*
Globulins	0.59*	0.68*	-0.57*	1.00	0.40*	0.47*	0.17	0.63*	0.54*
a1-globulins	0.49*	0.13	-0.44*	0.40*	1.00	0.14	-0.55*	0.20	0.49*
a2-globulins	0.42*	0.18	-0.36*	0.47*	0.14	1.00	-0.16	0.22	0.27
β-globulins	-0.36*	0.38*	0.22	0.17	-0.55*	-0.16	1.00	-0.12	-0.26
γ-globulins	0.59*	0.47*	-0.35*	0.63*	0.20	0.22	-0.12	1.00	0.53*
C-reactive protein	0.82*	0.20	-0.41*	0.54*	0.49*	0.27	-0.26	0.53*	1.00

Matrix of intercorrelations (r) of biochemical parameters of blood serum characterizing protein metabolism in dogs with gastroenteritis depending on presence of acute abdominal pain syndrome

Note: * – correlation dependence is significant ($p \le 0.05$; Spearman's test).

It was established that in dogs with acute gastroenteritis (Table 3), statistically significant correlations were formed between pain rating scale and biochemical parameters of blood serum, characterizing the proteinogram, namely: albumins, globulins, α 1-globulins, α 2-globulins, β -globulins, γ -globulins, C-reactive protein. In addition, serum concentration of total protein in sick animals significantly correlated with concentration of globulins, β -globulins and γ -globulins. Attention should be focused on presence of other correlations: between albumins and globulins, α 1-globulins, α 2-globulins, γ -globulins, C-reactive protein; between globulins and α 1-globulins, α 2-globulins, γ -globulins, C-reactive protein; between α 1-globulins and β -globulins, C-reactive protein; between γ -globulins and C-reactive protein. These changes confirm the significant pathogenetic role of systemic inflammation in the development of pain in the body of dogs with acute gastroenteritis. As a result of intercorrelation analysis (Table 4), pathogenetic relationships were established between the indicator of pain assessment scale in dogs with acute gastroenteritis and serum activity of ALT, AST, α -amylase, alkaline phosphatase, and serum creatinine concentration. Also, multiple significant correlations were established between the biochemical parameters of blood serum in sick dogs: ALT and AST, α -amylase, alkaline phosphatase; AST and creatinine; creatinine and cholesterol. The trend towards hypoalbuminemia in sick dogs can be explained by formation of secondary hepatopathy against the background of endotoxicosis. An increase in serum activity of alkaline phosphatase was associated with violation of motor function of bile ducts, alanine and aspartic aminotransferases — with the syndrome of cytolysis of hepatic and intestinal cells, creatinine concentration — with the development of pre-renal azotemia against the background of hypovolemia and dehydration of the body.

Table 4

Index	Pain Rating Scale	АЦТ	AST	a-amylase	Alkaline phosphatase	Urea	Creatinine	Cholesterol	β-lipoproteins
Pain Rating Scale	1.00	0.70*	0.39*	0.38*	0.83*	0.19	0.42*	0.25	0.03
ALT	0.70*	1.00	0.34*	0.34*	0.69*	0.15	0.11	0.17	0.12
AST	0.39*	0.34*	1.00	0.16	0.25	0.16	0.30*	0.08	0.22
α-amylase	0.38*	0.34*	0.16	1.00	0.26	0.04	0.02	0.12	0.19
Alkaline phosphatase	0.83*	0.69*	0.25	0.26	1.00	0.16	0.27	0.24	0.19
Urea	0.19	0.15	0.16	0.04	0.16	1.00	0.15	0.21	0.22
Creatinine	0.42*	0.11	0.30*	0.02	0.27	0.15	1.00	0.49*	-0.01
Cholesterol	0.25	0.17	0.08	0.12	0.24	0.21	0.49*	1.00	0.16
β-lipoproteins	0.03	0.12	0.22	0.19	0.19	0.22	-0.01	0.16	1.00

Matrix of intercorrelations (r) of biochemical parameters of blood serum in dogs with gastroenteritis depending on the presence of acute abdominal pain syndrome

Note: * - correlation dependence is significant (p≤0.05; Spearman's test).

Matrix intercorrelation analysis (Table 5) established pathogenetic relationships between the index of pain rating scale in dogs with acute gastroenteritis and serum concentration of tumor necrosis factor- α , interleukin-4, interleukin-6, interferon- γ , interleukin-1 α , interleukin-8. It is obvious that contamination, activation and increase in the number of living microbial cells of opportunistic bacteria in gastrointestinal tract of dogs with gastroenteritis causes the development of dehydration, intoxication and systemic inflammatory syndrome [3–8].

Table 5

Index	Pain Rating Scale	Tumor necrosis factor-α	Interleukin-4	Interleukin-6	Interferon-y	Interleukin-1α	Interleukin-8
Pain Rating Scale	1.00	0.86*	0.82*	0.92*	0.91*	0.85*	0.91*
Tumor necrosis factor-α	0.86*	1.00	0.83*	0.83*	0.88*	0.79*	0.82*
Interleukin-4	0.82*	0.83*	1.00	0.82*	0.84*	0.74*	0.86*
Interleukin-6	0.92*	0.83*	0.82*	1.00	0.89*	0.86*	0.92*
Interferon-y	0.91*	0.88*	0.84*	0.89*	1.00	0.78*	0.84*
Interleukin-1a	0.85*	0.79*	0.74*	0.86*	0.78*	1.00	0.83*
Interleukin-8	0.91*	0.82*	0.86*	0.92*	0.84*	0.83*	1.00

Matrix of intercorrelations (r) of blood cytokine profile parameters in dogs with gastroenteritis depending on the presence of acute abdominal pain syndrome

Note: * – correlation dependence is significant ($p \le 0.05$; Spearman's test).

We also found correlations between tumor necrosis factor- α and interleukin-4, interleukin-6, interferon- γ , interleukin-1 α , interleukin-8; between interleukin-4 and interleukin-6, interferon- γ , interleukin-1 α , interleukin-1 α , interleukin-8; between interleukin-6 and interferon- γ , interleukin-1 α , interleukin-8; between interleukin-1 α , interleukin-9; between interleukin-9; be

Conclusion

In the body of dogs with acute gastroenteritis, stable correlations are formed between the index of pain rating scale and pulse and respiration rate, hematocrit, erythrocyte sedimentation rate, the number of erythrocytes and leukocytes, serum concentration of albumins, globulins, α 1-globulins, α 2-globulins, β -globulins, γ -globulins, C-reactive protein, serum activity of alanine and aspartic aminotransferases, α -amylase, alkaline phosphatase and serum creatinine concentration, tumor necrosis factor- α , serum concentration of interleukin-4, interleukin-6, interferon- γ , interleukin-1 α , interleukin-8. These indicate activation of local and systemic immune-inflammatory response, formation of acute pain, intoxication, dehydration syndromes that occur against the background of changes in the motor, secretory, absorption, excretory function of the gastrointestinal tract. Dogs with gastroenteritis tend to develop secondary hepatopathy and pancreatopathy. Violation of intercorrelative relationships may indicate a violation of adaptivecompensatory reactions in the body in dogs with acute gastroenteritis. The parameters of cytokine profile of blood sera can be used as predictors of severity of pathological process and formation of acute abdominal syndrome in dogs with gastroenteritis.

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Патогенетические факторы, ассоциирующиеся с формированием острого абдоминального болевого синдрома собак при гастроэнтерите

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Аннотация. Исследовались интеркореллятивные связи между разнообразными клиническими и лабораторными показателями у собак, больных острым гастроэнтеритом. Показатель шкалы оценки боли достоверно (р ≤ 0,05) коррелировал с частотой пульса (r = 0,58), частотой дыхания (r = 0,50), гематокритом (r = 0,47), СОЭ (r = 0,72), количеством эритроцитов (r = 0,50) и лейкоцитов (r = 0,77), концентрацией альбуминов в сыворотке крови (r = -0,52), глобулинов (r = 0,59), α1-глобулинов (r = 0,49), α2-глобулинов (r = 0,42), β-глобулинов (r = -0,36), γ-глобулинов (r = 0,59), С-реактивного белка (r = 0,82), сывороточной активностью аланиновой (r = 0,70) и аспарагиновой аминотрасфераз (r = 0,39), α -амилазы (r = 0,38), щелочной фосфатазы (r = 0,83) и сывороточной концентрацией креатинина (r = 0,42), фактора некроза опухоли- α (r = 0.82), интерлейкина-4 (r = 0.92), интерлейкина-6 (r = 0.92), интерферона-у (r = 0.91), интерлейкина-1α (r = 0,85), интерлейкина-8 (r = 0,91). В организме собак, больных острым гастроэнтеритом, происходит активизация локальной и системной иммуновоспалительной реакции организма, возникает болевой, интоксикационный, дегидратационный синдром, происходят нарушения моторной, секреторной, всасывательной, экскреторной функции желудочно-кишечного тракта, формируется вторичная гепатопатия и панкреатопатия. Также констатировано наличие статистически значимых ($p \le 0.05$) коррелятивных связей между количеством эритроцитов и показателем гематокрита (r = 0,65), MCHC (r = 0,32), СОЭ (r = 0,35), концентрацией гемоглобина (r = 0,73) и количеством лейкоцитов (r = 0,35); между MCV и гематокритом (r = 0,62), MCHC (r = -0,64); между MCV и MCHC (r = 0,64); MCH и MCHC (r = 0,40); СОЭ и количеством лейкоцитов (r = 0,53). Изменения интеркоррелятивных связей между клинико-лабораторными параметрами у больных острым гастроэнтеритом собак можно рассматривать как предикторы тяжести патологического процесса.

Ключевые слова: острый гастроэнтерит, боль, патогенез, корреляция, воспаление, иммунология, гематология

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