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Treatment for cholangiohepatitis in cats

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Abstract. Acute bacterial cholangiohepatitis of cats is a common disease associated with the inflammation of bile ducts and liver parenchyma, characterized by development of a pronounced hepatodepressive syndrome (hypoalbuminemia), cytolysis (increase in serum activity of alanine and asparagine transaminase), cholestasis (increase in serum concentration of bilirubin, cholesterol, activity of alkaline phosphatase and gamma-glutamyltranspeptidase), intoxication, dehydration, mesenchymal-inflammatory and pain syndromes. The aim of the research was to study the effectiveness of treatment for acute bacterial cholangiohepatitis in cats with average severity of the pathology course. According to inclusion and exclusion criteria, the study included a cohort of cats (n = 12) with acute bacterial cholangiohepatitis. Clinical, hematological, ultrasonographic, statistical methods of investigation were used in this work. For sick cats with medium severity form of cholangiohepatitis, when administered as a complex therapy the combination of marbofloxacin, metronidazole, ursodeoxycholic acid, cyancobolamine, tocopherol acetate, infusion therapy also had a good therapeutic effect, which was accompanied by improved clinical and laboratory performance. In the blood of cats with cholangiohepatitis, in the background of intensive therapy, there was a significant decrease in white blood cell count, erythrocyte sedimentation rate, and in serum, there was an increase in albumin concentration, reduction of creatinine, aminotransferase activity, alkaline phosphatase, gamma-glutamyltranspeptidase, lipase.

Key words: cholangitis, hepatitis, effectiveness of treatment, analgesia, marbofloxacin, metrogyl, urodeoxycholic acid, lidocaine, maropitant, gabapentin

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

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Introduction

Pathology of small domestic animals with inflammatory and immune development mechanism is an urgent problem of veterinary medicine [1–3]. One of such diseases of cats is acute bacterial cholangiohepatitis [4–11]. This disease is characterized by development of inflammatory process in liver parenchyma and bile ducts, intoxication of organism, secondary changes in metabolism, formation of multimorbid pathology [12–16].

The treatment of sick cats with purulent cholangiohepatitis is based on antibiotics [17, 18]. It is necessary to isolate and identify pure culture of microorganisms of cholangitis pathogens and determine their sensitivity to antimicrobial agents. Various low-toxicity broad-spectrum antibiotics are used for effective treatment of sick cats, which provide sufficient concentrations in hepatobiliary system, in particular ampicillin, amoxicillin clavulanate, cephalexin, metronidazole, cephasolin, vancomycin, marbofloxacin and enrofloxacin.

The aim of the research was to study the effectiveness of complex treatment of cats with acute bacterial cholangiohepatitis, with average severity of the pathology course.

Materials and methods

The diagnosis for cholangiohepatitis of cats was made in a complex way taking into account the data of clinical examination, anamnesis, biochemical and morphological analysis of blood and ultrasonography [5, 7]. The following clinical criteria were used to assess the severity of the pathology: *mild form* — cats have clear consciousness, normal or subfebrile fever, reduced appetite, they actively and voluntarily change their posture and move around in space, vomiting is rare or absent, body dehydration syndrome is not pronounced; *medium form* — mental depression, marked weakness, subfebrile or pyretic fever, anorexia, rare vomiting, marked dehydration of the body; *severe form* — marked disorder of consciousness (severe oppression, stupor, sopor or coma), forced lying position, hypothermia, persistent anorexia, frequent vomiting, dehydration of the body is possible. Pain syndrome levels in animals were also assessed using a modified assessment scale [8].

General clinical blood analysis was performed using the URIT-2900 Vet Plus veterinary automatic hematology analyzer.

The BioChem SA semi-automatic biochemical analyzer (High Tecnology Inc., USA) was used to perform the above mentioned studies.

Ultrasound examination of abdominal organs was carried out on Aloka ProSound Alpha 6 (Japan) using a multi-frequency microconvection sensor with a scanning frequency of 6–9 MHz.

Cholecystocentesis for sick cholangiohepatitis cats was carried out under short-term multimodal anesthesia. The puncture of abdominal wall was performed on the right. Under aseptic conditions, cholecystocentesis was performed under ultrasound control

using a needle (22G, 0.7 × 40.0 mm) and 5 cm^3 syringe. The method of access was chipped [9]. As much bile as possible was aspirated into the syringe. The puncture site was treated three times with 70 % ethanol as an antiseptic and an operating field was used. At the end of the procedure, control ultrasonography of hepatobiliary system in experimental cats was performed to evaluate potential damage of gallbladder.

Cats with medium severity of cholangitis were also treated in two ways:

- group B1 marbofloxacin (Marfloxin®) in a dose of 2 mg/kg intramuscularly once a day for 14 days, metronidazole (Metrogyl®) in a dose of 15 mg/kg intravenously drops two times a day for 10 days with subsequent oral conversion to 15 mg/kg for another 20 days, ursodeoxycholic acid (Ursofalk®) orally in a dose of 15 mg/kg once a day for 30 days, Cyancobolamine (vitamin B_{12}) 500 µg subcutaneously once every 7 days for 30 days, alpha-tocopherol acetate (vitamin E) orally in a dose of 15 mg/kg two times daily for 6 weeks, infusion therapy with isotonic crystalloid solutions in a daily volume of 100 ml (0.9 % sodium chloride solution — 40 ml, 5 % glucose solution — 30 ml and yonosteryl — 30 ml);
- group B2 — animals to whom therapy of similar group B1 was carried out, but with an additional prescription for 5 days of multimodal analgesia (lidocaine infusion with a constant rate of 50 µg/kg/hour, maropitante (Cerenia®) intravenously drops in a dose of 1 mg/kg once a day and gabapentin in a dose of 20 mg/kg two times a day orally. Treatment of cats with cholangiohepatitis should be comprehensive considering severity of the pathology, using pharmacological means of etiotropic, pathogenetic, symptomatic and substitution therapy.

For comparison of two or more groups, whose digital indicators did not correspond to the normal distribution of features, we used the non-parametric Mann — Whitney U-criterion for independent samples or the Wilcoxon test for dependent groups, respectively. To calculate the reliability of the difference in groups by the frequency of occurrence of features, criterion χ^2 was used, and if necessary, with the correction of Yates. The difference between numerical indicators was considered reliable at $p < 0.05$. All calculations were made on a personal computer using a statistical program STATISTICA 7.0 (StatSoft, USA).

Results

Bacteriological retrospect studies in five cats suffering from cholangiohepatitis with medium severity of pathology. The monoculture of *Escherichia coli* was isolated from bile; for seven cats it was associated with *Pseudomonas aeruginosa*, *Proteus vulgaris*, *Proteus mirabilis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Staphylococcus epidermidis* or *Streptococcus faecalis*. All selected cultures have a high sensitivity to marbofloxacin.

The effectiveness of treatment measures was assessed on 12 cats with medium severity of cholangiohepatitis. Experienced cats were divided into two groups, in particular: B1 (n = 5) — animals who were treated with marbofloxacin (Marfloxin®) in a dose of 2 mg/kg intramuscularly once a day for 14 days and with metronidazole (Metrogyl®)

in a dose of 15 mg/kg intravenously two times a day for 10 days, followed by oral conversion to a similar dose for another 20 days, ursodeoxycholic acid (Ursofalk®) orally in a dose of 15 mg/kg once daily for 30 days, cyancobolamine 500 μg subcutaneously once every 7 days for 30 days, alpha-tocopherol acetate orally in a dose of 15 mg/kg two times daily for 6 weeks, infusion therapy was also prescribed with isotonic crystalloid solutions in daily volume of 100 ml (0.9 % sodium chloride solution — 40 ml, 5 % glucose solution — 30 ml and yonosteryl — 30 ml); and B2 (n = 7) — animals, which were treated with similar group B1, but with an additional prescription for 5 days of multimodal analgesia (lidocaine infusion with a constant rate of 50 μg/kg/hour, maropitanate (Cerenia®) intravenously drops in a dose of 1 mg/kg once a day and gabapentin in a dose of 20 mg/kg two times a day orally).

The results of treatment of cats with medium severity of cholangiohepatitis are given in Table 1.

Table 1

Results of treatment for medium severity cholangiohepatitis in cats

Results of treatment	Groups of animals				Confidence of the difference p
	B1		B2		
	Number of cases	Percentage, %	Number of cases	Percentage, %	
Full recovery	2	40.0	4	57.1	≤1
Clinical recovery	1	20.0	1	14.3	≤1
Enhancement	1	20.0	1	14.3	≤1
Recidivism	0	0	1	14.3	≤0.5
Lethal	1	20.0	0	0	≤0.5
Total	5	100	7	100	—

Full recovery in cats with medium severity cholangiohepatitis was observed in B2 group by 17.1 % more frequently than in B1 group. In group B2, one case of recurrence of the pathology was registered, while in group B1, no such cases were found. At the same time, one lethal case was registered in group B1 and made up 20.0 %. It should be emphasized that the specified intergroup variability of outcomes at the medium severity of cholangiohepatitis in cats was found to be unreliable due to low number of observations.

Reduction of oppression in animals from group B1 was observed on 7…12 days of treatment, in group B2 — on 5…10 days; cessation of vomiting and full recovery of appetite was observed in group B1 on 7…12 days of therapeutic measures, in group B2 — on 6…9 days. During the repeated examination of sick cats in the veterinary clinic, an increase in general activity of animals, absence of painfulness at palpation of abdominal cavity was stated. The hiccups of visible mucous membranes in animals of groups B1 and B2 gradually decreased and became almost invisible on the 6th day.

In cats of B1 group on the 5th day of therapy, the index of the modified scale of pain syndrome estimation was on the average 15.0 ± 1.22 points, and in cats of B2 group this index was 5.1 ± 0.51 points, that was revealed to be reliable (Mann —Whitney criterion, $p < 0.01$).

Rectal body temperature in cats at the end of the therapy period ranged from 38.1 to 39.1 °C. Thus, according to the results of the clinical study of cats at the end of the

therapy, improvement of the clinical condition in most cats with cholangiohepatitis was found. Persistent improvement in cats of B1 group occurred on 10.0 ± 1.05 days, and in cats of B2 group — 6.3 ± 0.56 days. The above mentioned difference was revealed to be reliable ($p < 0.05$) at Mann — Whitney test.

The indices of erythrocytopoiesis during the period of cats' therapy at cholangiohepatitis of medium severity showed the normalization of hemopoiesis processes and elimination of hemoconcentration phenomena (Table 2).

Table 2

General clinical indicators of blood in cats with medium severity of cholangiohepatitis during the treatment

Indicator	Clinically healthy (n = 11)	Scheme	Before treatment		After treatment	
			n	M ± m	n	M ± m
Leukocytes, 10^9/L	7.9 ± 0.63	B1	5	11.8 ± 1.72	4	8.6 ± 0.71
		B2	7	18.0 ± 5.42	7	8.8 ± 0.53
Hemoglobin, g/L	135.4 ± 6.63	B1	5	155.2 ± 14.23	4	150.8 ± 9.64
		B2	7	117.0 ± 14.00	7	140.9 ± 4.91*
Erythrocytes, 10^{12}/L	8.6 ± 0.22	B1	5	10.0 ± 0.55	4	7.4 ± 0.44*
		B2	7	7.2 ± 0.52	7	7.8 ± 0.42
Hematocrit, %	39.9 ± 1.55	B1	5	46.5 ± 4.02	4	40.9 ± 2.84
		B2	7	35.2 ± 4.00	7	52.3 ± 1.69*
MCV, μm^3	46.8 ± 2.53	B1	5	46.8 ± 2.58	4	56.3 ± 5.20
		B2	7	48.9 ± 3.45	7	52.9 ± 2.82
MCH, pg	15.8 ± 1.05	B1	5	15.2 ± 0.98	4	20.7 ± 1.90*
		B2	7	16.4 ± 1.23	7	18.4 ± 1.14
MCHC, g/L	337.5 ± 6.11	B1	5	333.4 ± 8.39	4	349.3 ± 8.83
		B2	7	332.0 ± 4.89	7	334.0 ± 9.84
RDW, %	16.0 ± 0.48	B1	5	15.4 ± 0.47	4	16.0 ± 1.05
		B2	7	14.4 ± 0.81	7	15.3 ± 0.70
Thrombocytes, 10^9/L	259.9 ± 17.5	B1	5	184.8 ± 13.98	4	337.8 ± 34.26
		B2	7	325.4 ± 79.28	7	304.0 ± 24.96
MPV, μm^3	9.7 ± 0.23	B1	5	8.3 ± 0.28	4	8.5 ± 0.23
		B2	7	9.9 ± 0.50	7	8.8 ± 0.25*
ESR, mm/hour	4.3 ± 0.52	B1	5	17.8 ± 3.50	4	9.0 ± 1.29
		B2	7	23.4 ± 3.90	7	6.6 ± 1.02*

Note. The difference between the digital indicators was considered significant at $p < 0.05$ (*).

The number of erythrocytes in the blood of cats treated according to B1 circuit decreased significantly (by 1.35 times; $p < 0.05$), the MCH index increased (by 1.2 times; $p < 0.05$), there was a tendency for the reduction of COE. In peripheral blood of cats of B2 group at the end of therapy, there was a reliable increase of hemoglobin concentration (by 1.2 times; $p < 0,05$), decrease of MPV (in 1.13 times; $p < 0.05$) and ESR (by 3.55 times; $p < 0.05$), a tendency of MCH increase close to reliability. In the blood of animals of both groups, a decrease in the number of leukocytes was observed close to reliability.

Dynamics of changes in the course of treatment of serum biochemical parameters in cats with cholangiohepatitis of medium severity is given in Table 3.

Table 3

Biochemical indicators of cat blood serum at medium severity of cholangiohepatitis during the treatment

Indicator	Clinically healthy (n = 11)	Scheme	Before treatment		After treatment	
			n	M ± m	n	M ± m
Urea, mmole/ L	7.8 ± 0.37	B1	5	8.4 ± 1.09	4	7.1 ± 0.49
		B2	7	9.1 ± 0.95	7	6.8 ± 0.30
Creatinine, μmol/L	122.5 ± 8.18	B1	5	131.8 ± 6.14	4	85.8 ± 8.24*
		B2	7	140.1 ± 10.04	7	86.3 ± 3.94*
Total bilirubin, μmol/L	3.5 ± 0.41	B1	5	12.4 ± 10.30	4	2.4 ± 0.54
		B2	7	23.1 ± 9.00	7	3.3 ± 0.39
AST, U/L	35.9 ± 3.33	B1	5	97.3 ± 22.13	4	45.5 ± 6.30
		B2	7	44.8 ± 5.82	7	47.4 ± 3.39
ALT, U/L	42.7 ± 3.32	B1	5	89.6 ± 18.45	4	47.0 ± 6.98
		B2	7	88.8 ± 19.46	7	52.1 ± 5.03
SF, U/L	21.3 ± 2.5	B1	5	39.0 ± 7.13	4	21.0 ± 1.73
		B2	7	59.3 ± 18.40	7	21.7 ± 1.78*
GGT, U/L	0.4 ± 0.15	B1	5	4.2 ± 1.80	4	2.3 ± 1.31
		B2	7	4.9 ± 1.16	7	2.4 ± 0.75
Glucose, mmole/ L	4.7 ± 0.16	B1	5	5.8 ± 1.13	4	4.6 ± 0.23
		B2	7	6.3 ± 1.24	7	3.9 ± 0.23
Total protein, g/ L	72.1 ± 1.58	B1	5	77.0 ± 4.82	4	72.1 ± 2.89
		B2	7	74.1 ± 6.28	7	68.3 ± 1.50
Albumins, g/ L	25.7 ± 0.78	B1	5	20.9 ± 1.89	4	26.8 ± 0.75*
		B2	7	22.2 ± 1.51	7	28.0 ± 0.87*
Cholesterol, mmole/l.	2.8 ± 0.16	B1	5	4.4 ± 0.38	4	2.8 ± 0.13*
		B2	7	3.9 ± 0.44	7	2.9 ± 0.16*
Amylase, U/L	736.3 ± 48.7	B1	5	846 ± 87	4	658 ± 74
		B2	7	781 ± 53	7	724 ± 64
Lipase, U/ L	38.0 ± 4.64	B1	5	79.6 ± 19.21	4	32.3 ± 10.62
		B2	7	66.1 ± 10.99	7	35.0 ± 5.38*

Note. The difference between the digital indicators was considered significant at $p < 0.05$ (*).

In serum of cats of B1 group the concentration of creatinine (1.53 times; $p < 0.05$) and cholesterol (1.57 times; $p < 0.05$) was significantly reduced, albumin concentration was increased (1.28 times; $p < 0.05$). In animals of B1 group a trend of decrease in serum activity of ALT, AST, alkaline phosphate, amylase and lipase, which is close to reliability, was also revealed. In serum of cats of B2 group the concentration of creatinine (by 1.62 times; $p < 0.05$) and cholesterol (by 1.34 times; $p < 0.05$) was significantly reduced, albumin concentration increased (by 1.26 times; $p < 0.05$), lipase activity decreased (by 1.88 times; $p < 0.05$) and alkaline phosphorus (by 2.73 times; $p < 0.05$). In animals of B2 group there was also revealed a close to reliable downward trend in serum activity of ALT, AST, GGT and amylase. Additional prescription of multimodal analgesia to cats with medium cholangiohepatitis leads to a reliable ($p < 0.01$) decrease of the modified pain scale indicator by 2.9 times.

Discussion

Sick cats with medium severity form of cholangiohepatitis, when administered as a complex therapy the combination of marbofloxacin, metronidazole, ursodeoxycholic acid, cyancobolamine, tocopherol acetate, infusion therapy had a good therapeutic effect, which was accompanied by improved clinical and laboratory performance. However, additional prescription of means of multimodal analgesia (gabapentin, lidocaine, maroapitan) was accompanied by increase of frequency of full recovery of animals, reliable decrease of signs of pain syndrome.

Gabapentin is an analogue of the inhibitory neurotransmitter of gamma-aminobutyric acid in the central nervous system. This preparation has a blocking effect on chronic pain impulse [4, 6]. Intravenous lidocaine injection in the form of infusion at a constant rate has a pronounced analgesic effect in cats [5]. Maropitant is a powerful and selective antagonist of neurokinin-1 receptor antagonists, influences the production of substance P, has a powerful anti-emetic, moderate sedative and analgesic effect. The experiment also shows some anti-inflammatory effect of this medicinal substance [10, 18].

In the blood of cats with acute bacterial cholangiohepatitis in the background of intensive care, there was a significant decrease in SER, the number of white blood cells; and in the serum, there was an increase in the concentration of albumin, a decrease in the concentration of creatinine, albumin, the activity of aminotransferases, schF, GGT, lipase. Relatively low lethality rates of cats in our study can be explained by the exception of chronic (lymphocytic-plasmocytic) forms of cholangiohepatitis. According to literature data, chronic lymphocytic cholangiohepatitis in cats is a rather severe pathology, which has a long latent period and almost always ends with biliary cirrhosis development [12, 15].

Conclusion

Sick cats with medium severity form of cholangiohepatitis, when administered as a complex therapy the combination of marbofloxacin, metronidazole, ursodeoxycholic acid, cyancobolamine, tocopherol acetate, infusion therapy had a good therapeutic effect, which was accompanied by improved clinical and laboratory performance. However, the additional prescription of multimodal analgesia was accompanied by an increase in the frequency of complete recovery of animals and a reliable decrease in the signs of pain syndrome. In the blood of cats with acute bacterial cholangiohepatitis in the background of intensive therapy, there was a significant decrease in SEE, white blood cell count; and in serum, there was an increase in albumin concentration, reduction of creatinine, albumin, activity of aminotransferases, alkaline phosphate, GGT, lipase. Additional prescription of multimodal analgesia (gabapentin, lidocaine, maroapitan) for sick cats leads to a significant decrease in the modified pain scale.

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Лечение кошек при холангиогепатите

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Аннотация. Острый бактериальный холангиогепатит кошек представляет собой чрезвычайно распространенную патологию, связанную с воспалением паренхимы печени и желчных протоков, характеризующуюся развитием гепатодепрессивного синдрома (гипоальбуминемии), цитолиза (повышение активности аспарагиновой и аланиновой трансаминазы в сыворотке крови), холестаза (повышение сывороточной концентрации билирубина, холестерина, активности гамма-глутамилтранспептидазы и щелочной фосфатазы), интоксикации, дегидратации, мезенхимально-воспалительного и болевого синдромов. Цель исследования — изучить эффективность лечения кошек с острым бактериальным холангиогепатитом при средней степени тяжести течения патологии. Согласно критериям включения и исключения в исследование проводили на группе кошек (n = 12) с острым бактериальным холангиогепатитом. Использовали клинические, гематологические, ультразвуковые, статистические методы исследования. У больных кошек при средней форме холангиогепатита при назначении в составе комплексной терапии комбинация метронидазола, марбофлоксацина, урсодезоксихолевой кислоты, токоферола ацетата, цианкоболамина при инфузионном введении оказывала хороший терапевтический эффект, что сопровождалось улучшением клинико-лабораторных показателей. В крови кошек

с холангиогепатитом на фоне интенсивной терапии наблюдалось достоверное снижение количества лейкоцитов, скорости оседания эритроцитов, а в сыворотке крови — повышение концентрации альбумина, снижение активности аминотрансферазы, гамма-глутамилтранспептидазы, щелочной фосфатазы, липазы, концентрации креатинина.

Ключевые слова: холангит, гепатит, эффективность лечения, анальгезия, марбофлоксацин, метрогил, уродезоксихолевая кислота, лидокаин, маропитант, габапентин

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