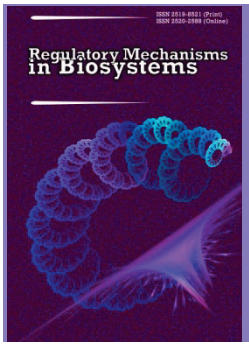

Regulatory Mechanisms in Biosystems

ISSN 2519-8521 (Print)
ISSN 2520-2588 (Online)
Regul. Mech. Biosyst.,
2020, 11(2), 266–271
doi: 10.15421/022039

Macronutrient status and indicators of acid-alkaline blood balance in cats with chronic renal failure

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Article info

Received 19.04.2020
Received in revised form 10.05.2020
Accepted 12.05.2020

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Holovakha, V. I., Mostovyi, E. V., Sliusarenko, A. O., Piddubnyak, O. V., Suslova, N. I., & Matsinovich, M. S. (2020). Macronutrient status and indicators of acid-alkaline blood balance in cats with chronic renal failure. Regulatory Mechanisms in Biosystems, 11(2), 266–271. doi:10.15421/022039

Chronic renal failure is a common pathology among cats. According to various literary sources, this pathology is found in 0.5–14.0% of cats. Pathology in cats in our studies is a consequence of glomerulonephritis. The diagnosis of chronic renal failure established on the basis of clinical, instrumental, and laboratory methods of blood and urine testing. Studies have found that chronic renal failure in cats is clinically characterized by apathy, anorexia, dry skin, odor of urea, vomiting, thirst, occurrence in the mouth of uremic ulcers (9.5% of patients), tachycardia (up to 177 beats per minute) tachypnoea (up to 45 respiratory movements per minute), hypertension. In the urine – hyposthenuria, erythrocyturia, leukocyturia, kidney epithelium, hyaline and granular cylinders. According to echosonography – increase in echogenicity of the parenchyma, brain substance echone negative, cortico-brain differentiation erased. In the blood test – normochromic macrocytic anemia, thrombocytopenia, hyperazotemia (up to 27.9 mmol/L), hypercreatininemia (324 μmol/L), hyperuricemia (615 μmol/L), 4.6-fold increase in SDMA (symmetric dimethylargin). In chronic renal failure, cats have a significant change in the elemental composition of the blood. In particular, the Na^+ content was increased by 3%, Ca^{2+} 1.6 times, P 2.1 times. Instead, the K^+ level was reduced 1.9 times. Changes in acid-base equilibrium (ABE) were also detected: the pH decreased to 7.22; HCO_3^- by 34%, total CO_2 by 32.3%, while anionic difference (AG) and buffer bases (BE) increased by 1.8 and 3.5 times, respectively. Such changes are characteristic of the development of lactic acidosis. The obtained experimental data on changes in mineral metabolism and acid-base equilibrium in the serum of cats in chronic renal failure supplement and clarify information on the pathogenic pathology of the kidneys in cats aged 5–10 years. Blood biochemical data can be used to improve early-stage diagnostics without clinical manifestations of chronic renal failure, their prevention and treatment, and to solve applied scientific problems in the field of nephrology and urology of small animals.

Keywords: buffer bases; water-ion exchange; hyperphosphatemia; biomarker; symmetric dimethylarginine.

Introduction

The stability of the composition and structure of the internal environment of the body is a prerequisite for maintaining the life of animals (Hall et al., 2015). They depend on the condition of many organs and systems, including kidneys. Kidneys function mainly to maintain consistency in fluid volume and composition (Littman, 2011). They perform excretory, regulatory and endocrine functions. In acute and chronic kidney disease, the animal develops renal failure, which is acute and chronic (Bartges, 2012; Bradley et al., 2019). Acute renal failure occurs suddenly due to acute renal involvement, accompanied by a decrease or complete cessation of urinary output (Syme et al., 2006; Szczepankiewicz et al., 2019). Acute renal failure occurs due to the use of antibiotics, cytostatics (methotrexate, cyclophosphamide, etc.), non-steroidal anti-inflammatory drugs, ethylene glycol, excess calcium, phosphorus (Dobenecker et al., 2018; Brunetto et al., 2019); hypo- and hypermagnesemia (Van den Broek et al., 2018; Chacar et al., 2019); poisoning with salts of zinc, arsenicum, plumbum, cuprum, shock phenomena, disseminated blood coagulation syndrome, hyperparathyroidism (Geddes et al., 2018), salmonellosis, leptospirosis, etc. (Dobenecker et al., 2018; Colakoglu et al., 2019) consequences (Chen et al., 2019). Severe renal failure manifests uremia with auto-intoxication, delay in the body of nitrogen metabolites and other toxic substances that disrupt water-salt, acid-base and osmotic homeostasis, with secondary metabolic disorders in tissues and dystrophy of tissues and dysfunction of all organs and systems in general (Robert et al., 2004; Marino et al., 2014). As a result of renal failure, the death of the animal occurs (King et al., 2007; Conroy et al., 2019). Chronic renal failure is a pathological condition characterized by impaired renal regulation of the body's chemical homeostasis, with partial or complete impairment of urine formation and excretion due to a decrease in glomerular filtration rate (Lees et al., 2005; Polzin, 2011). Chronic renal failure develops gradually as a result of progressive irreversible loss of a functioning renal parenchyma (Vientós-Plotts et al., 2015; Maniaki & Finch, 2018). This disrupts the glomerular and tubular functions of the kidneys, develops uremia, which leads to changes in water-ion and osmotic homeostasis (Jepson et al., 2007). Chronic renal failure occurs in cats of all ages. Cats are more prone to this disease than dogs and get ill from the age of 5. This problem has not been sufficiently studied in domestic literature. The purpose of the experimental work was to establish changes in water-ionic and acid-base blood balance in cats in chronic renal failure. Clarifying this issue will assist veterinary medicine professionals in developing early diagnosis techniques and new treatment protocols for chronic renal failure to improve cats' clinical status and extend their life span.

Materials and methods

The experimental part of the study was performed on cats (n = 21), patients with chronic renal failure, aged 5–10 years (breeds: British, rowing

(short-haired), Persian, Siamese and breedless) and clinically healthy (n = 10). In the course of the experimental studies, all manipulations with experimental animals involved in the experiment were carried out in accordance with the European Convention on the "Protection of Vertebrate Animals Used for Experimental and Scientific Purposes" (Strasbourg, 1986) and the "General Ethical Principles of Experiments on Animals", approved by the First National Congress on Bioethics (Kyiv, 2001) and adherence to the principles of humanity set out in the European Community Directive. In the study of cats, we used basic clinical methods (examination, palpation, auscultation, thermometry) and special (tonometry, echosonography, laboratory methods of blood and urine). The pulse rate was determined using an EdanVE-100B pulse oximeter (Biovet, Ukraine). Tonometry was performed using a PetMAP graphic II veterinary tonometer (Biovet, Ukraine) on the thorax and tail. The cuff was used 3.0–3.5 cm in size. Measurements were made from three to five times, after which the device displayed an average value of measurements (Nabity et al., 2015). An important method for determining chronic renal failure is ultrasound examination of the kidneys. This method is highly informative, painless. With ultrasound sonography it is possible to determine most pathologies of the urinary system and identify structural changes in organs related to their location, size, shape and structure. Ultrasound shows focal changes in the kidneys, cysts, tumors, concretions.

In the blood, the number of erythrocytes, platelets, hemoglobin, hematocrit, "red" blood indices (MCH and MCV) was determined using a Mindray BC-2800Vet (China) hematology analyzer.In serum, using the automatic biochemical analyzer Mindray BS120 (China), the content of total protein, albumin, urea, creatinine, uric acid, calcium (Ca^{2+}), phosphorus (P^{5+}) (Cormy reagents, Poland) was determined. Sodium (Na^{+}), potassium (K^{+}), chlorine (Cl^{-}) and acid-base equilibria were determined in stabilized blood (Li-heparin): pH, HCO_3^{-}, anionic difference (AG), partial pressure of carbon dioxide, buffer bases (BE), total CO_2 (tCO_2) was determined using the Idexx Laboratories: IdexxVetStat Electrolyte and Blood Gas Analyzer, (USA) microprocessor complex for 5 minutes after blood collection. These indices were determined by the method of optical fluorescence from discrete sensors. SDMA content was determined in serum on a BionoteVchech V200 analyzer (SD Biosensor, Korea).

Urine for the study was obtained by cystocentesis. Puncture of the bladder was performed by puncturing the abdominal wall and bladder in order to obtain "clean" urine. This selection technique prevents the contamination of the microflora from the lower urinary tract and changes in the physical properties of the urine, which can be owned by natural selection. The manipulation was performed under the control of a Mindray DP10 ultrasound apparatus (China) and 2 and 5 mL syringes. Animals were fixed in the ventro-dorsal position (on the back). An ultrasound linear sensor was placed over the bladder area above the bladder (the area of the last third of the abdomen, about 5 cm from the pubic fusion). Next to the sensor marker, the puncture site was treated twice with ethyl alcohol. After puncture on the ultrasound, the location of the needle and the depth of the injection were observed on the apparatus screen. After visualization, needles in the bladder were aspirated punctate. During the introduction of the needle in the syringe a negative pressure is created on the urine. After urine was collected, the needle was removed in one sharp motion. At the puncture site, no urine flow was monitored using the instrument. Urine express-diagnostics were performed using a Kelilong electron RHS-300ATC veterinary Refractometer (China), DIRUI H-10 test strips (Dirui industrial, China) and cytology of urine sediment. For microscopic examination of urine sediment, it was pre-centrifuged on a laboratory centrifuge CM-3 (Ukraine) with a speed of up to 4000 rpm. Urine centrifugation was performed for 5 min then the supernatant was drained and the precipitate was examined under a BioBLueLabLED microscope (Euromex, Netherlands) at ×400 magnification. Statistical processing of the results was performed using Statistica 10 (StatSoft Inc., USA, 2011). A Bonferroni-corrected ANOVA was used to determine the difference between the samples.

Results

Apathy, anorexia, dryness of the skin, dehydration, odor of urea, vomiting, and thirst were noted in the sick cats. The body temperature in most cats with chronic renal failure was normal, only increased in 14.2% by 0.5–1.0 °C. The mucous membranes of the mouth and eyes were pale pink, rarely anemic. In 9.5% of sick cats in the mouth there were uremic ulcers. The pulse rate increased 1.3 times, averaging 163 beats per minute, and the respiratory rate per minute increased almost twice, to 45 compared with healthy animals. Arterial systolic pressure increased 1.2 times and averaged 158.0 mmHg, and diastolic pressure increased 1.1 times and amounted to 106.0 mmHg, compared with healthy animals.In the study of urine in cats revealed hypostenuria. The relative urine density was 1.005–1.020 g/mL, pH 6.0–7.5. In a precipitate of urine erythrocytes, leukocytes, cells of renal epithelium, hyaline, granular cylinders, mucus.

In sonography, anatomically, the kidneys were located correctly, not enlarged in size (85.7%), reduced (14.3%). The borders were level (76.2%), hilly (23.8%). The thickness of the parenchyma of the left kidney was 3.0–4.5 mm, the right one is 3.0–4.2 mm. The pelvis and proximal part of the ureter are not enlarged. The echogenicity of the parenchyma was increased. Brain substance was echonegative, cortico-brain differentiation smoothed or erased (Fig. 1). The circulation was satisfactory.

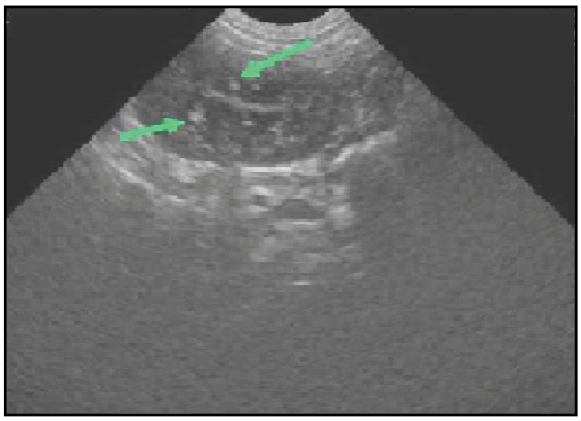

Fig. 1. Structure of the kidney of cats with chronic renal failure: arrows indicate hyperechoic inclusions

In a blood test, hemoglobin content in cats with chronic renal failure averaged 96.4 g/L, 1.5 times lower than clinically healthy ($P < 0.001$). It should be noted that oligochromia (less than 100 g/L) was established in 61.9% of diseased animals. In others, blood pigment values were lower than normal. The number of erythrocytes in cats in the average group was 6.5×10^{12}/L ($P < 0.001$), that is, was normal (6.5×10^{12}/L – lower limit of normal). A detailed analysis of the results showed that in the majority of animals (61.9%) the number of erythrocytes was below the minimum level. The main indicator of the evaluation of erythrocytopoiesis is hematocrit. In pathological animals, the average of erythrocytopoiesis averaged 27.1%, which is 19.6% less than in clinically healthy animals ($P < 0.001$). The index of MCH in diseased cats did not differ from the values of clinically healthy ones (Table 1). Only 19.0% of diseased cats had hypochromia (i.e. low values of MCH).

Table 1
Dynamics of indicators of erythrocytopoiesis in cats in chronic renal failure

Indexes	Clinically healthy (n = 10)		Clinically ill, (n = 21)	
	x ± SE	Lim	x ± SE	Lim
Ep., 10^{12}/L	8.9 ± 0.24	7.9–9.8	6.5 ± 0.19***	4.93–8.14
Hb, g/L	146 ± 1.71	139–152	96.4 ± 2.61***	74–117
MCH, pg	16.4 ± 0.51	14.2–19.2	15.4 ± 0.36	12.8–19.1
Ht, %	46.7 ± 0.69	42.7–49.2	27.1 ± 1.02***	19.9–42.1
MCV, μm^3	52.7 ± 1.86	45.4–59.5	43.5 ± 1.56*	29.6–5.3

Note: * – $P < 0.05$; *** – $P < 0.001$ relatively clinically healthy animals.

Index – MCV, in sick animals averaged 43.5 μm^3 ($P < 0.05$), which is 17.5% less than in clinically healthy ones. Microcytosis (less than 45 μm^3) was detected in 66.7% of sick animals. The results of studies in cats with chronic renal insufficiency indicate anemia, which should be characterized as normochromic microcytic.

The number of platelets in cats with chronic renal failure averaged 272×10^9/L, which is 35.5% less than in clinically healthy ones (Fig. 2).

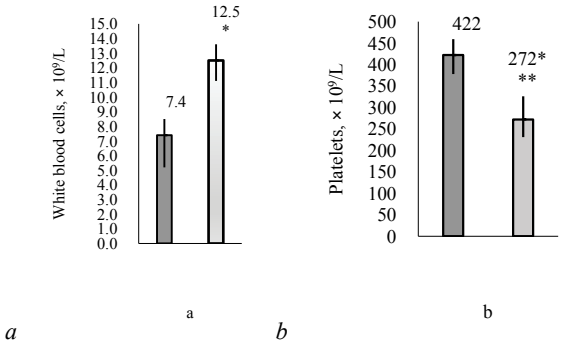

Fig. 2. The content of cellular elements of blood in cats with chronic renal failure: *a* – leukocytes, clinically healthy, 12.5 × 10^9/L (n = 10, x ± SE), * – P < 0.05; *b* – platelets, clinically ill, 272 × 10^9/L (n = 21, x ± SE), *** – P < 0.001

It should be noted that decreased values of platelets (below 300 × 10^9/L) were found in 85.7% of sick animals. Thrombocytopenia is a consequence of the destruction of "blood" plates by antibodies against microbial factors. The number of leukocytes in cats averaged 12.5 × 10^9/L, i.e. 68.9% higher than in clinically healthy ones (P < 0.001; Fig. 2). However, it should be noted that the total number of leukocytes did not go beyond physiological fluctuations. The animals of the experimental group showed significant changes in the dynamics of the serum biochemical spectrum due to chronic renal failure. Their total protein content averaged 78.3 g/L, up 21.6% compared to clinically healthy animals (P < 0.01; Table 2).

Table 2
Dynamics of total protein and blood albumin in cats with chronic renal failure

Groups of animals	Total protein, g/L		Albumini, g/L		Albumini, %	
	x ± SE	Lim	x ± SE	Lim	x ± SE	Lim
Clinically healthy, n = 10	64.4 ± 1.04	59.7–71.5	29.8 ± 0.57	27.8–33.4	46.3 ± 0.19	45.5–46.9
Clinically ill, n = 21	78.3 ± 0.78**	71.6–85.8	31.2 ± 0.70	25.4–36.7	39.9 ± 0.90**	33.8–48.2

Note: ** – P < 0.01 relatively clinically healthy animals.

It should be noted that hyperproteinemia (greater than 75 g/L) was detected in 90.5% of animals. It is relative and related to the dehydration of the cat's body. It is impossible to evaluate the state of the protein-synthesizing function of hepatocytes without determining the fractional composition of the total protein and, in particular, albumin, since these proteins are synthesized in the liver. The absolute amount of these finely dispersed proteins in diseased animals did not differ from the clinically healthy values on average, and averaged 31.2 g/L. Instead, the relative proportion of albumin in the structure of total protein was 39.9%, which is 6.4% less than in clinically healthy cats (P < 0.01).

Therefore, in chronic renal failure, hypoalbuminemia is indicated, indicating hepatopathy. In addition, hypoalbuminemia, apparently, indicates changes in the epithelium of the renal tubules of the proximal department in the form of protein dystrophy, which causes a resorptive deficiency of the vacuolar-lysosomal system and the system of the basal labyrinth of tubules with increased glomerular filtration. In the living body in the process of protein biosynthesis is the reverse process – the splitting of proteins, which is enhanced by various pathologies. The final products of protein metabolism are non-protein nitrogenous components, including urea, uric acid, creatinine and the like. These residual nitrogen components are, for the most part, markers of the functional state of nephrons. The content of urea in the serum reflects the balance between the rate of its synthesis in liver cells and the rate of excretion of the kidneys with water. The urea content in the blood of animals of the experimental group with chronic renal failure averaged 21.7 mmol/L, which is 2.5 times higher than in clinically healthy animals (P < 0.001; Table 3).

High levels of urea indicate a decrease in the rate of glomerular filtration in the kidneys. In patients with chronic renal failure, increased values of the marker of the filtration capacity of nephrons – creatinine, were found. Its content in the serum of sick cats averaged 324 μmol/L, which is 2.7 times higher than in clinically healthy animals (P < 0.001; Table 3). That is, cats have a glomerular filtration volume of about 23 mL/min. The decrease in the filtration capacity of the glomerulus of the kidneys causes the development of uremic syndrome. Scientists believe that the pathology of the kidneys initially raises the level of another component of residual nitrogen, uric acid, because the filtration in the glomerulus of the kidneys of substances with a higher molecular weight is impaired. These include uric acid. The content of this product of residual nitrogen in the serum of cats with chronic renal failure was 614.5 μM/L, which is 4.4 times higher than clinically healthy animals (P < 0.001; Table 4). Hyperuricemia (an increase in uric acid content in the blood) indicates a decrease in glomerular filtration and a decrease in tubular secretion.

Table 3
Dynamics of indices of residual nitrogen in the blood of cats in chronic renal failure

Groups of animals	Urea, mmol/L		Creatinine, μmol/L		Uric acid, μM/L	
	x ± SE	Lim	x ± SE	Lim	x ± SE	Lim
Clinically healthy, n = 10	8.6 ± 0.41	6.1–10.7	119 ± 5.8	91–142	140 ± 6.8	107–177
Clinically ill, n = 21	21.7 ± 0.63***	18.5–27.9	324 ± 7.8***	269–397	615 ± 13.3***	497–741

Note: *** – P < 0.001 relatively clinically healthy animals.

In diseased cats, the level of SDMA in the blood was on average 4.6 times higher than in the clinically healthy ones (P < 0.001; Fig. 3).

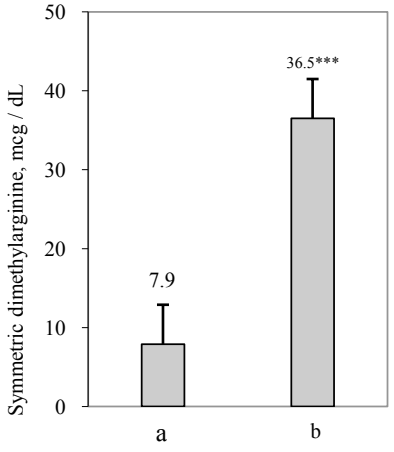

Fig. 3. SDMA content of 36.5μg/dL (n = 21, x ± SE): *** – P < 0.001 in cats in chronic renal failure, compared with healthy animals

In chronic renal failure, cats have impaired water-ion exchange. The content of sodium (Na^+) in the serum of cats was 158.6 mmol/L, which is 3% more than in clinically healthy animals (P < 0.05; Table 4).

Table 4
Dynamics of macronutrients in the serum of cats in chronic renal failure

Indexes	Clinically healthy, n = 10		Clinically ill, n = 21	
	x ± SE	Lim	x ± SE	Lim
Na^+, mmol/L	154 ± 1.0	150–160	159 ± 1.5*	142–172
K^+, mmol/L	4.4 ± 0.23	3.6–5.4	2.3 ± 0.11***	1.7–3.4
Ca^{2+}, mmol/L	2.4 ± 0.05	2.1–2.7	3.9 ± 0.06***	3.4–4.4
P^{5+}, μmol/L	1.2 ± 0.04	1.0–1.4	2.6 ± 0.06***	2.1–3.0
Cl^-, μM/ L	123 ± 1.1	118–127	121 ± 0.7	116–129

Note: * – P < 0.05; *** – P < 0.001 relatively clinically healthy animals.

Hypernatremia indicates impaired filtration function of nephrons. The content of the other macronutrient – potassium (K^+), on the contrary, was reduced. On average, its level in the group was 2.3 mmol/L, which is 1.9 times less than in clinically healthy cats (P < 0.001; Table 4). Chlorine (Cl^-) content in the serum of cats in chronic renal failure did not change compared to clinically healthy values (P < 0.05; Table 4). The kidneys play an important role in maintaining calcium homeostasis (Ca^{2+}) and phosphorus (P^{5+}). Chronic renal failure in cats is often caused by a violati-

on of mineral status. The content of Ca^{2+} in the blood of cats in chronic renal failure in the average group was 3.9 mmol/L, i.e. 1.6 times higher than in clinically healthy animals ($P < 0.001$; Table 5). Hypercalcemia is apparently due to the development of chronic metabolic acidosis, since reduced renal mass limits the renal excretion of ammonium, the major buffer for H^+ secretion, and the buffer action catalyzes the absorption of calcium salts. Increased calcium in the cerebral circulation is associated with hyperparathyroidism, which causes uremic encephalopathy. In sick animals, increased values of phosphorus (P^{5+}) in the serum were detected. On average, the macronutrient content of clinically ill cats was 2.55 mmol/L, which is 2.1 times higher than in clinically healthy animals ($P < 0.001$). Hyperphosphatemia reduces the renal production of calcitriol in the proximal tubules, inhibits the activity of 1α-hydroxylase, which promotes the conversion of $25(OH)D_3$ to $1,25(OH)_2D_3$. The last metabolite of cholecalciferol ($1,25(OH)_2D_3$) is vitamin D, a binding protein that is transported to target cells in the intestine and the bone tissue, where it reacts with nuclear receptors. The result of this interaction is the phosphorylation of the receptor complex, which activates specific genes under the control of which enterocytes form calcium-binding protein (CBP), alkaline phosphatase, actin, Ca-ATPase.

In the practice of veterinary medicine experts are increasingly paying attention to the acid-base balance. All metabolic processes in cells are related to the production of carbon dioxide (carbon dioxide), hydrogen ions and oxygen consumption. To maintain the constancy of the internal environment of the body it is necessary that the pH levels of carbon dioxide and oxygen in the blood be maintained within fairly clear limits. Fluctuations in blood pH compatible with life are ± 0.4 units. A slight fluctuation in pH in one direction or another can cause inhibition of enzyme activity, alteration of the degree of electrolyte dissociation, impaired central nervous system activity, and the like. Supports acid-base homeostasis of the body buffer systems of blood and tissues, intracellular metabolism, during which hydrogen ions are used and lungs produce CO_2; the kidneys produce HCO_3^- and secrete H^+ in the form of NH_4^+ and H_2PO_4. The blood pH of cats with chronic renal failure averaged 7.22, which is 2.2% less than in clinically healthy animals. Low pH (below 7.35) was found in all sick animals ($P < 0.01$; Table 5). Reduced pH values in cats with chronic renal failure indicate the development of metabolic acidosis. In maintaining acid-base homeostasis of the body an important role is played by the hydrocarbonate buffer system. In its stability, kidneys supply an additional amount of bicarbonate ions, which counterbalance the formation of hydrogen ions in the body, and play an important role.

Changes in the concentration of HCO_3^- (bicarbonate) are mainly the result of metabolic disorders in the body and renal decompensation. In cats with chronic renal failure the concentration of HCO_3^- averaged 13.8 mmol/L, which is 34.0% less than in clinically healthy animals ($P < 0.001$; Table 5).

Table 5

Indicators of acid-base balance in the blood of cats with chronic renal failure

Indexes	Clinically healthy, n = 10		Clinically ill, n = 21	
	x ± SE	Lim	x ± SE	Lim
pH	7.38 ± 0.004	7.37–7.40	7.22 ± 0.004**	7.19–7.25
Bicarbonates, mmol/L	20.9 ± 0.17	20.2–21.8	13.8 ± 0.30***	12.0–17.1
pCO_2, mmHg	38.0 ± 0.33	37.0–40.0	36.5 ± 0.64	33.0–43.0
Anionic difference, mmol/L	14.3 ± 0.41	12.2–15.8	25.6 ± 1.69**	12.8–39.6
Buffer basics (BE), mmol/L	–3.5 ± 0.21	–2.41–4.27	–12.3 ± 0.31***	–8.85–14.33
Total CO_2, mmol/L	22.0 ± 0.18	21.3–22.9	14.9 ± 0.31***	13.0–18.3

Note: ** – $P < 0.01$; *** – $P < 0.001$ relatively clinically healthy animals.

An indicator of ABQ is the anion gap (AG), which is calculated by the values of bicarbonate concentration (HCO_3^-) and blood levels of electrolytes: sodium (Na^+), potassium (K^+), and chlorine (Cl^-). With the help of AG we can detect disorders of acid-base equilibrium (ABQ), and primarily metabolic acidosis. This indicator for acidic phenomena increases, and can decrease (rarely). In the animals of the experimental group, the anionic difference (AG) averaged 25.6 mmol/L, which is 1.8 times higher compared with clinically healthy animals ($P < 0.01$; Table 5). Another indicator of disorders of acid-base balance in cats with chronic renal failure is BE (buffer bases) – an excess or deficiency of buffer bases. This indicator represents the difference between the actual buffer base concentration and the normal buffer base concentration. The content of BE in the blood of diseased animals averaged –12.3, which is probably higher than the clinically healthy ones ($P < 0.001$; Table 5). BE allows you to estimate the amount of metabolic disorders or the value of metabolic compensation. In cats, with chronic renal failure, there are increased values of BE, which indicates the accumulation in the blood of not only hydrochloric acid (HCl), but also lactate, that is, the development of lactate acidosis. Cats with chronic renal insufficiency have low values of total carbon dioxide (tCO_2). The mean for the tCO_2 group was 14.9 mmol/L, which is 32.3% less than in the clinically healthy ones ($P < 0.001$). Reduction in the total carbon dioxide (tCO_2) in the blood indicates impaired metabolic processes in cats and the occurrence of acidosis.

Discussion

Chronic renal failure (CRF) is an irreversibly progressive clinical syndrome that limits the ability of the kidneys to excrete substances in the urine, regulate acid-base balance and perform endocrine functions (Langston, 2004; Braun, 2005; Sobolev, 2011). It is a consequence of glomerulonephritis, pyelonephritis, kidney amyloidosis, leptospirosis, polycystic kidney disease, hydronephrosis and the like. According to various authors, chronic renal failure occurs in 0.5–14.0% of cats (Kuwahara et al., 2006; Jepson et al., 2009; Polzin, 2010). According to our research, the animals with pathology were cats from 5 to 10 years of age, who showed glomerulonephritis. Diagnosis of chronic renal failure was made by clinical examination, echosonography and laboratory methods of urine and blood examination. The most indicative markers for diagnosis were blood biochemical tests – urea, creatinine, uric acid, and the SDMA (symmetric dimethylarginine) biomarker (Hall et al., 2014a; Nabity et al., 2015). The content of urea in the serum was increased 2.5 times, indicating impaired excretory function of nephrons.

In chronic renal insufficiency, the filtration function of the glomerular nephron apparatus is significantly reduced, as indicated by the serum creatinine content, which was 2.7 times higher than in clinically healthy animals. Violation of the filtration function of the glomerulus of the kidneys causes the development of uremia. However, in recent years, scientists have come to believe that an earlier test that indicates a violation of the filtration capacity of nephrons is the presence of substances with a higher molecular weight. These include uric acid because it has a higher molecular weight than urea and creatinine (Levchenko et al., 2019).

Hyperuricemia indicates a decrease in glomerular filtration and tubular secretion. The content of urea in sick cats was more than 4 times higher than in clinically healthy animals. In the last few years, scientists have preferred the earliest diagnostic test to determine chronic renal failure – symmetrical dimethylarginine (SDMA) (Polzin et al., 2000; Hall et al., 2014b; Nabity et al., 2015; Turitsyna & Kazakova, 2015; Levchenko et al., 2019; Le Sueur et al., 2019). This innovative biomarker is an amino acid that is formed by the cleavage of methylated proteins, correlates with glomerular filtration rate (GFR) and is completely excreted by the kidneys (Nabity et al., 2015; Hall et al., 2016). Therefore, the SDMA is considered to be a more accurate indicator of the glomerular filtration rate (GFR). The content of SDMA in the blood by chronic renal failure was 4.6 times higher than in clinically healthy animals. The renal lesion is indicated by urine indices. Hypostenuria is established in sick cats. In the precipitate of urine there are erythrocytes, leukocytes, hyaline and granular cylinders, cells of the renal epithelium. In cats with chronic renal failure hypertension is manifested, which is a consequence of changes in the kidney parenchyma, which leads to fluid retention, changes in blood pressure. Hypertension can be exacerbated by changes in the concentration of sodium ions (Na^+) and endocrine disorders, in particular, the parathyroid hormone has a cardiotoxic effect, which contributes to the increase of anemia, impaired cholecalciferol metabolism. Analyzing the indicators of "red" blood we found that cats with chronic renal failure showed normocytic microcytic anemia. This is confirmed by erythrocyte indices (the lowest values were found in 61.9% of animals), hemoglobin content (oligochromemia in 61.9%), hematocrit (19.6% lower than in clinically healthy animals) and indices of red blood – MCH (the majority of patients (81%) were normal)

and MCV (reduced values were found in 66.7% of patients). Anemia was found in all pets due to chronic renal failure. This is due to a lack of erythropoietin (this hormone is synthesized in the juxtaglomerular nephron apparatus and causes the formation of red blood cells in the red bone marrow), a deficiency of the ferrum, which leads to a decrease in erythrocyte activity. Thrombocytopenia was established in the animals of the experimental group, which is apparently a consequence of an increase in activated and degranular platelets, indicating an increased aggregation (gluing) and a decrease in glomerular filtration (Kushnir, 2014).

A study of the macronutrient composition in the serum revealed the following: Na^+ (sodium) content was higher than in clinically healthy ones, which is evidence of impaired nephron filtration function. The K^+ (potassium) content was reduced 1.9-fold compared to clinically healthy ones. Hypokalemia, apparently, is evidence of the presence of renal tubular acidosis of the distal and proximal type and impaired reabsorption of Na^+ (sodium) in the proximal tubules, increasing it in the distal, which ultimately causes their loss of K^+ (potassium). Patients with chronic renal insufficiency showed hypercalcemia (Ca^{2+} content 1.6 times higher than clinically healthy ones), which indicates the development of chronic metabolic acidosis and uremic encephalopathy. In cats with chronic renal insufficiency hyperphosphatemia was revealed in the serum, which contributes to the inhibition of calcitriol synthesis in the tubular apparatus and activity of 1α-hydroxylase, which leads to the progression of imbalance of remodeling processes with the predominance of resorption and reduced. That is, hyperphosphatemia is evidence of the development of renal osteodystrophy (Shvarcz, 2002; Geddes et al., 2018).

In recent years, veterinary experts have been paying enough attention to the definition of acid-base balance (ABQ), especially in severe internal pathology, including nephropathy. This is due to the fact that the metabolism in the tissues of the body is closely linked to the formation of carbon dioxide (carbon dioxide), hydrogen ions (hydrogen) and the consumption of oxygen (oxygen). Acid-base balance (acid-base equilibrium) provides tissue buffer systems and intracellular metabolism, which uses hydrogen ions and the lungs excrete carbon dioxide. Bicarbonate (HCO_3^-) is synthesized in the kidneys and they excrete hydrogen (H^+) in NH_4^+ and H_2PO_4 compounds. The first indicator of the acid-base balance of blood (ABQ) is the hydrogen index of blood (pH), which in clinically healthy cats was 7.38. In patients, it was 2.2% less, indicating the presence of metabolic acidosis. Its presence is confirmed by the values of bicarbonate (HCO_3^-), which were on average 1.5 times lower than in healthy animals. Low values of bicarbonate indicate reduced conversion in renal tubules from bicarbonate of carbon dioxide and low activity of carbonic anhydrase of proximal tubules and secretion of hydrogen ions (H^+) from cells into the lumen of tubules in exchange for Na^+, which is intensified. An indicator that indicates acidic phenomena in cats in chronic renal failure is the anion gap (AG). In renal pathology in cats its values increased 1.8 times higher than in clinically healthy animals. Also, the diagnostic criterion for assessing acid-base balance disorders is BE. The BE parameter indicates the amount of acid or alkali required to titrate 1 L of blood to a pH of 7.4 at pCO_2 of 40 mm Hg, a temperature of 37 °C, and complete saturation of hemoglobin with oxygen. With regard to total CO_2 (tCO_2), carbon dioxide (CO_2) is a product of cellular respiration metabolism. It is transported into the bloodstream to the lungs and excreted. Carbon dioxide is available in two forms: 90% as bicarbonate (HCO_3^-) and 10% as carbonic acid (H_2CO_3). The kidneys and lungs are responsible for regulating carbon dioxide, carbonic acid and bicarbonate in the blood. Decrease in tCO_2 causes impaired respiratory function due to respiratory acidosis and asphyxia, damage to the nervous system through hypercapnia and acidemia.

Conclusions

In cats with chronic renal failure, the etiologic factor of which was glomerulonephritis, there are significant changes in the macronutrient status and acid-base equilibrium. Hypernatremia, which indicates a violation of the filtration capacity of nephrons, was found in sick animals. The content of the other K^+ (potassium) macronutrient was, on the contrary, reduced (1.9 times compared to clinically healthy ones). Hypocalcaemia is evidence of tubular acidosis of the distal and proximal type. The content of Cl^- (chlorine) in cats with chronic renal failure did not change compared with clinically healthy animals. That is, Cl^- in patients with cats with chronic renal failure compensates for the effect of Na^+ (sodium) in the extracellular fluid. In cats with chronic renal insufficiency hypercalcemia, which indicates the development of chronic metabolic acidosis, has been established. Hyperphosphatemia (phosphorus content 2.1 times higher than clinically healthy ones) was found in patients, which contributes to the reduction of calcitriol production and the enzyme 1α-hydroxylase, which causes impaired D-vitamin metabolism. In cats, with chronic renal failure, significant changes in acid-base equilibrium were found. In particular, patients have lowered pH (an average of 7.22 which is 2.2% less than in healthy cats). Cats with chronic renal failure were found to have 34% lower bicarbonate (HCO_3^-). In patients, cats showed elevated (1.8 times) values of AG (anionic difference) and buffer bases (BE), which indicates the development of lactic acidosis.

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