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Information Condition of the Liver of Dogs at Pathologies at the Reproductive Period of Ontogenesis

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Abstract: In the study the method of assessing adaptive and regenerative opportunities of the liver by assessing of its information state was applied. The research revealed achange in the nature of the information state of the tissue of the liver at hepatoadenoma, liver cancer and non-cancer pathologies. Discovered changes of the information parameters characterizing the liver, indicate various kinds of adaptive processes in the organ. It is shown that at the non-neoplastic diseases of the liver, tissue system uses the existing structural adaptation resources, but it tends tocollapse. Changes of the information parameters were more pronounced at malignant disease than at hepatoadenoma, it is revealed reduction of system reliability to negative value. When tumors of the liver, tissue system is simplified, ordered and directed the growth and increase the reliability, such system complicates the possibility of successful treatment of the organ in such pathologies.

Key words: Entropy · Biosystem · Liver Pathology · Adaptation

INTRODUCTION

Liver diseasesin dogscan have very diverse symptoms, as liveris an important intermediate organ of the metabolism which is involved in many physiological processes of an organism (digestion, detoxificationand hemopoiesis).

About 80% of casesof hepatopathyare associatedwith kidney diseases of gastrointestinal tract,pancreas andthe central nervoussystem. Liver diseasemay be primaryorsecondary. The liver has highadaptation reservesandregenerative abilities. The liver dysfunctions in the majority of cases are subclinical, with no pronounced symptoms andbecause ofthe regenerative functions of the organitre covers quickly without the need of medical intervention.

The defeat of 70-80% of functional liver cells results in hepatic insufficiency. Suchdiseases can be acuteorchronic. If at a disease of a liver doesn't come recovery, it develops fibrosis or cirrhosis of liver and irreversible terminal hepatic insufficiency [1, 2].

Primary liver neoplasmasin the dogsare infrequent, with an estimated prevalence in necropsystudies in 0.6-2.6% of cases. Liver metastases at dogs are much more frequent than primary hepatic tumors and affect 30.6-36.8% from all animals with non-hepatic neoplasm.The spleen, pancreas and gastrointestinal tract are the most common locations of primary tumors implicated in such metastases. Metastatic disease is more common and occurs two and a half times more frequently than primary liver tumors in dogs, particularly from primary cancer of the spleen, pancreas and gastrointestinal tract [3, 4]. The liver can also be involved in other malignant processes.

The four basic categories of primary malignant hepatic tumors in dogs are: hepatocellular, bile duct, neuroendocrine (or carcinoid) and mesenchymal. There are three morphologic types of these primary hepatic tumors: massive, nodular and diffuse. Massive liver tumors are defined as large, solitary masses confined to a single liver lobe; nodular tumors are multifocal and involve several liver lobes; and diffuse involvementmay

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represent the final stage of neoplastic disease with multifocal or coalescing nodules in all liver lobes or diffuse effacement of the hepatic parenchyma. The prognosis for cats and dogs with liver tumors is determined by histology and morphology. The prognosis is good for massive hepatocellular carcinoma (HCC) and for benign tumors because complete surgical resection is possible and biologic behavior of these tumors is relatively nonaggressive. In contrast, the prognosis is adverse for dogs with malignant tumors other than massive HCC [5-8].

Changes in pre-and postnatal development of mammals in normal and pathological conditions are increasingly considered as a phenomenon caused by the dynamics of adaptation and regeneration capabilities of living systems at different hierarchical levels [9-12]. To assess the parameters of ability of adaptation and regeneration proposed to use Shannon entropy and its derivatives of tissue parameters. Information state of the tissue is an indicator of adaptive capacity of biosystem [13-15].

Several authors do not exclude the existence of aninterrelationbetween change of information state of system and the development of pathological processes in the period of appreciable senile changes [16-22]. It is shown that in case of damage andadaptation responses in biological systems occurs a redistribution of energy-flow accompanying the process of restructuring the tissue. Smallnumbers of publications examinethe information condition of organs andtissues [23-27].

From the above, it seems actual to study the information status of the liver as an organ providing homeostasis in dogs at normal and at a hepatocellular adenoma (HCA), hepatocellular carcinoma (HCC) and non-cancer diseases.

MATERIALS AND METHODS

Animals: Were examined H&E histologicalslides of a dog liver with various pathological processes.Age of the animalswas 5-7years.

The diagnosis is based on data of postmortem and histological examination.

Were investigatedthe following slides:

- Normal liver (n = 150);
- At cirrhosis (n=88);
- At chronic hepatitis (CH) (n=80);
- At HCA(n=79);
- At HCC(n=87).

Studies Ofthe Information Condition of the Systemof the Liver: To determine the information statusat focal lesions of the liver, pieces of tissue were taken from the least altered areas on the border of macroscopically distinct lesions. In case of visual homogeneity of organ material was taken from any part of it.

Based on the concept of information in a tissue systemlike the displaying of the diversity of morphology and function of the process, for assessing the information status of organs and tissues have been proposed and tested the such indicators - information morphological capacity (H_{max}), information morphological entropy (H), information morphological organization (S), the relative morphological entropy (h) and redundancy (R) [28-31].

In this case, the baseline characteristics, which were used to calculate these parameters, can vary widely (the linear dimensions of the structures, their number, etc.). In our study was defined the volume of the nuclei of hepatocytes.Volume of the nuclei of hepatocytes was measured by image analyzer "Videotest" at H&Eslides.

It was carried outa breakdown ofthe aggregateof the measuredvolumesof nuclei ofhepatocytes into classes.

Information morphological capacity H_{max}, which means the maximum structural diversity,was calculated by formula [28-31]:

$$H_{max}=\log_2 n,$$

where n - number of classes of volumesof hepatocyte nuclei.This parameter isdefined bya particularcharacteristic (hepatocyte nuclei volume) remains constant for atissue or organdescribedinthe normal and pathologies.

Next, we made the calculation of the real structural diversity H. Real structural diversity is the parameter that clearly illustrates the degree of determinism of morph functional system in time and space [28-31]. The calculation was made using the formula:

$$H=-\Sigma P_i \log_2 P_i,$$

whereΣP_i is the sum of probabilities of stay of the measured parameter of cells in one of existing classes; $\log_2 P_i$ - logarithm of the probability of staying in one of the possible classes. In this case, the value of P_i is defined as the classical probability [5].

Knowing the maximum and actual structural diversity, we can calculate the organization of the system (S), the difference between the maximum possible and the real structural diversity (implemented structural diversity).

This parameter, in our opinion, displays the state of the system adaptability to date. To determine the value of this parameter was used the formula [28-31]:

$$S=H_{max}-H.$$

It is necessary to consider that when $H = H_{max}$, the system is deterministic, but such relation to the vast majority of permissible is possible only in theory. Then we determined the coefficient of relative entropy of the system, or (the coefficient of compression of information) h by Avtandilov and Avtandilov and Areshidze *et al*. [28-31]:

$$h=H/H_{max}.$$

High levels of relative morphological entropy provide an evidence of the disorder of the system and significantly reducing of its structural integrity [18-20].

The coefficient on the relative organization of the system (redundancy factor) R is given by Avtandilov and Areshidze *et al*. [28-31]:

$$R=(S/H_{max})\times 100\%.$$

With these data, the researcher has the opportunity to calculate the equivocation of the system (the value of reliability) ***e*** [28-31]:

$$e=(H_p-H_n)/H_{max},$$

where H_n - real structural diversity in normal, H_p - real structural diversity in pathology.

Statistical Analysis: Values are expressed as mean (± SD). The statistical analysis was performed using one-way analysis of variance (ANOVA). The statistical difference determined using repeated measures analysis of variance or paired Student t-tests. A p value of < 0.05 was considered statistically significant.

RESULTSAND DISCUSSION

Liverof healthy dogswas characterizedby such parameters:H_{max}was3.32±0.0003bit,rate of Hwas equal to2.552±0.014bits, respectively, S was 0.7658±0.0014b it, h - 0.7687±0.0044 bit (Fig. 1), R equaled 23.13±0.45% (Fig. 2).

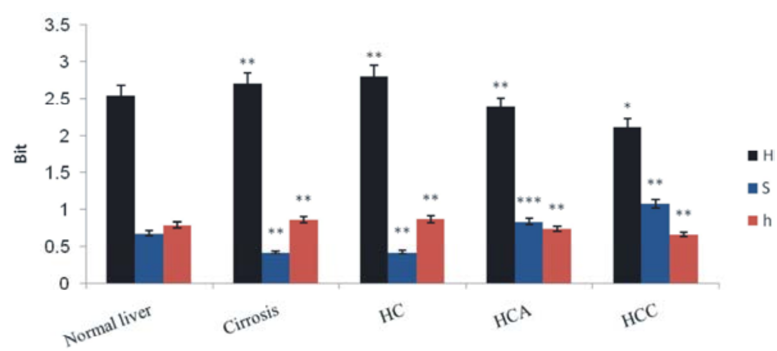

Fig. 1: Magnitude of the H, S and h in normal liver of dogs, liver with HCA, HCC and non-cancer diseases. Statistical significance was assessed using student t-test. *** indicates P<0.001, ** indicates P<0.01, * indicates p<0.05.

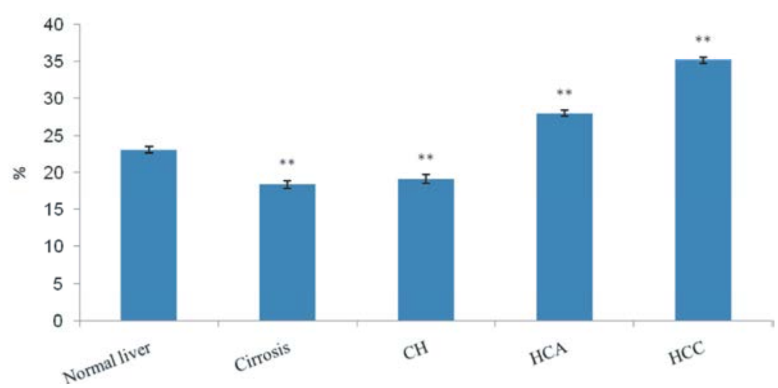

Fig. 2: Value of the R index at the liver in normal liver of dogs, liver with HCA, HCC and non-cancer diseases. Statistical significance was assessed using student t-test. *** indicates P<0.0005, ** indicates P<0.005, * indicates p<0.05.

AtHC the value of H increased to 2.680±0.077 bits, S reduces the 0.638±0.077 bits, h is increased to 0.8078±0.0057 bit and R reduced to 19.22±0.57%. The value of ***e*** was 0.130 ± 0.017.

A character of difference from the norm of the information of the dog liver with cirrhosis was similar. H is 2.707±0.018 bits, S was equal to 0.6130±0.018 bits, h reached 0.8154±0.0056 bit, R reduced to 18.46±0.56% *and* ***e***was 0.1550± 0.013.

At HCA we observed decrease of H concerning to the normal to 2.391±0.013 bits. Accordingly, the value of S was higher than normal - 0.929±0.013 bits, h reduced to 0.7202±0.004 and R increased to 27.98±0.4%. Index ***e*** was-0.161 ± 0.0009.

At HCC the value of H concerning to the norm dropped substantially, making 2.151±0.013 bits, the value of S increases significantly to 1.169±0.013 bits, h reduced to 0.6479±0.004 bits, R increases up to 35.21±0.40% and ***e*** was-0.401±0.023.

Thus, changes of the information parameters characterizing the liver indicate various kinds of adaptive processes in the organ.

At the non-neoplastic diseases of the liver it was observedthe increase of the H, which means an increase of the entropy of system, in parallel with this process itwas observed an increase of information compression, as evidenced by increase of coefficient of the relative entropy of the system (h). In addition, it was observed the decrease of the structural diversity of the system (S) and the coefficient of excess (R), which mean the number of redundant structural elements of the system.

Changes of information system at a cancer of a liver were different. In particular, there was a decrease of both total and relative entropy of the system against the increase of its structural diversity and the coefficient of redundancy. At the same time, changes of the information parameters were less pronounced at hepatoadenoma than at malignantdisease.

CONCLUSIONS

Thus, at non-neoplastic diseases of the liver, tissue system uses existing structural adaptation resources, the level of structural diversity of the system reduces, the number of redundant structural elements is also reducing and it is a tendency to destroying the integrity of the system. At tumors there is a simplification of the information system of the liver and as a consequence, increase of its reliability, ordering, is observed the tendency to system growth, which may testify to the compensatory-adaptive reactions in the organ.

At tumors the liver tissue system is simplified, ordered and directed to the growth and decrease of the reliability of such system complicates the possibility of successful treatment of the organ in such pathologies.

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