



Current Approaches to Hormonal Therapy in Animals with Immuno-Mediated Arthritis

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Abstract

The article presents the results of studies about the development of an integrated approach to therapy of immuno-mediated arthritis in animals. It was found out that the use of corticosteroids (in particular, prednisolone) is effective in treating arthritis of dogs, but side effect of prolonged use of the drug can lead to hepatic impairment. Considering this, constant monitoring of animals' liver condition with biochemical blood tests and ultrasound is necessary. For prescribing a course of treatment it is rational to use preparations with hepatoprotective action that increase the functional capacity of liver cells to synthesize, detoxify and eliminate various xenobiotic substances and also stimulate regeneration of hepatocytes. One can adequately use glucocorticosteroids and achieve the desired therapeutic effect with the least negative impact on body guided by above-mentioned parameters.

Key words: veterinary pharmacology, animals, arthritis, therapy, glucocorticosteroids, hepatoprotectors.

INTRODUCTION

Arthritis is a variety of inflammatory joint diseases, affecting synovial membranes, articular cartilage, capsule and other articular elements. One form of this pathology is an immune-mediated arthritis caused by the actions of somebody's own immune system [1,2].

The treatment of immuno-mediated arthritis in animals is still remains one of the most complex problem of veterinary medicine and requires a comprehensive approach to therapy with anti-inflammatory and chemotherapeutic drugs application. Glucocorticosteroids, widely used for this purpose, are still the most effective anti-inflammatory drugs, because they actively suppress the inflammatory focus, blocking the production of mediators of inflammation, enhance the action of other drugs, relieve swellings, reduce the sense of pain and have an immunomodulatory effect [3-5].

Glucocorticosteroids (GCS) are steroid hormones that are produced in the adrenal cortex. The term "glucocorticoid" emphasizes the ability of these hormones to stimulate gluconeogenesis and the deposition of glycogen in liver. Two hormones are synthesized in the adrenal cortex: cortisone and hydrocortisone (cortisol). Cortisone is a biologically active compound that can be converted into hydrocortisone in liver. This term also applies to semisynthetic drugs, such as prednisolone, dexamethasone, etc [6,7].

Prednisolone is a hormonal agent that is a dehydrated analogue of a hydrocortisone, which is often used in clinical practice for the immuno-mediated arthritis pharmacotherapy and is considered as a standard drug. As for glucocorticoid activity, it is 5 times stronger than hydrocortisone and refers to drugs with an average duration of action.

At the same time, the problem of drug-induced hepatotoxicity acquires particular relevance in modern medicine, which is convincingly evidenced by the frequency of registered side effects in various drugs,

including those of the GCS. There are data in scientific literature that synthetic estrogens and 17-substituted steroids with a long course of administration can lead to pathological changes in liver function and may be inducers of cholestasis [8].

The aim of the research was to study of liver condition of dogs after prolonged use of GCS and to develop approaches to reducing their hepatotoxic effect in the therapy of immuno-mediated arthritis in animals.

METHODOLOGY OF RESEARCH

Dynamic research was conducted by a comparative aspect over a 3-year period in two stages:

1. Study of dog's liver with prolonged use of GCS;
2. Development of approaches for reducing the hepatotoxic effect of prednisolone in the treatment of immuno-mediated arthritis in animals.

48 dogs of different breeds and sex were selected for the formation of groups, whose age varied in a range of 5-6 years and weight category from 12 to 17 kg. The diagnosis of immune-mediated arthritis was determined based on history, clinical signs, x-ray examination of joints and specific laboratory tests (cytological and bacteriological study of synovial fluid).

Clinical methods were used to evaluate the condition and behavior of an animal, palpation was performed, the measurement of circumference and the volume of joint movements, the body weight of animals was determined. Laboratory methods were used to assess systemic inflammatory processes according to the parameters of hematological examination (ESR, hemoglobin, erythrocytes and leukocytes, as well as their rod and segment-nuclear forms). Local inflammatory-degenerative processes in joints were examined by the level of total cytosis and qualitative cellular composition of cellular elements of the joint cavity contents. Morphometric examination of joint tissues was also performed.

All animals were observed with ultrasound diagnostics of the abdominal cavity, including liver as well as biochemical blood test for the content of hepato-indicator enzymes: alanine aminotransferase (ALT), aspartate aminotransferase (ALAT) and alkaline phosphatase (ALP).

After background studies dogs with a basic diagnosis of immune-mediated arthritis but with concomitant liver pathology were excluded from the experiment.

Dogs in the groups were in similar living conditions with the same feeding program during all periods of the research. All animals were observed by several courses of treatment with prednisolone (the duration of the course was 30 days, the maximum daily dose of 0,5 mg per 1 kg of body weight was given orally 2 times a day for 3 weeks, the abolition was effected by a gradual decrease in the dose for 10 days). In addition, chondroprotectors and physiotherapy were prescribed, anesthetics were used if necessary.

In the second stage of the study the first experimental group of dogs (n = 12) in addition to the basic treatment got hepatoprotector, including essential phospholipids, methionine and silymarin which was individually set 2 times a day (with a total daily dose of 0,3 ml per 1 kg of body weight) monthly courses with a break for 2 weeks. The second group of dogs (n = 12) was a control, where the treatment of immuno-mediated arthritis in animals passed without the use of hepatoprotective drugs.

RESULTS

It was found out that all animals (n = 24) had positive dynamics in the treatment of immuno-mediated arthritis at the first stage of the studies, when assessing the condition of dogs that had been treated with prednisolone for a long time. However, in 18 dogs (75%), moderate hepatomegaly was detected during the assessment of the liver boundaries, with no sharp pain, while an ultrasound examination revealed pathological changes in the liver such as "hepatosis".

In a biochemical study in the blood of dogs, with signs of dystrophic processes in the liver, changes were observed indicating hepatocellular leakage and cholestasis (Table 1). As a result of data evaluation, it was determined that in the content of indicator enzymes in the blood of dogs there were significant changes in the concentrations of these indicators in the direction of increase from physiological norm by the end of the experiment. Upon completion of the studies, the amount of ALT exceeded the background level by 44%, the difference in AST was 32,2%. Registered hyperphosphatasemia indicated moderate cholestasis of animals (content was detected at 112,5-4,2 U/l, slightly exceeding the norm).

Table 1 - Biochemical parameters of dogs' blood, with prolonged therapy with GCS (prednisolone)

Indicators	Background	End of experiment	Norm
ALT, U/l	43,6±1,3	62,8±2,1*	15-58
AST, U/l	34,5±1,9	45,6±1,4*	16-43
AP, U/l	83,1±3,5	112,4±3,2	10-100

Note: * - the confidence level $P \leq 0,05$ in relation to the control

The results of the second stage of the studies showed that the treatment of immuno-mediated arthritis in dogs with additional use of hepatoprotective agents neutralized the hepatotoxic effect of GCS.

In dogs of the first experimental group the clinical examination showed no painfulness in liver and no increase in its size, ultrasound examination revealed no pathological changes in the structure of the organ. In 7 control animals (58.3%) symptomatic signs of hepatosis were revealed.

Dynamics of biochemical parameters of dogs' blood (Table 2) testified to the effective influence of hepatotropic therapy on the level of ALT, AST and AP- their concentration corresponded to the parameters of the normal range, which indicates the absence of cytolytic syndrome and cholestasis.

Determination of the activity of aminotransferases in control animals showed that the average concentration of ALT in the group was $69,4 \pm 1,8$ U/l, AST – $44,7 \pm 2,6$ U/l by the end of the experiment. Thus, in dogs without the use of hepatoprotectors, enzymatic activity of aminotransferases was at a higher level than in animals of the experimental group with a significant difference of 31,7% (for ALT) and 25,9% (for AST).

Table 2 - Biochemical parameters of dogs' blood at the end of the experiment, with prolonged therapy with prednisolone (M ± m; n = 12)

Indicators	Groups		Norm
	Experimental	Control	
ALT, U/l	52,7±1,3*	69,4±1,8	15-58
AST, U/l	35,5±2,5*	44,7±2,6	16-43
AP, U/l	96,9±4,2	108,6±3,9	10-100

Note: * - the confidence level $P \leq 0.05$ in relation to the control

The average value of alkaline phosphatase in control dogs exceeded the normal range by 12,1% in relation to the first group of animals with a difference at the trend level.

CONCLUSION

Thus, based on the study, it can be concluded that the use of corticosteroids (particularly prednisolone) is effective in treating arthritis of animals, but the side effects of drugs with prolonged use can lead to a worsening of the liver condition. Consequently, animals that receive long-term GCS, regardless of dose, require monitoring of the liver with biochemical blood tests and ultrasound.

Moreover, using hormonal therapy for immuno-mediated arthritis in animals, it is rational to apply additional preparations of hepatoprotective action, that increase the functional capacity of liver cells to synthesize, detoxify and excrete various xenobiotic substances, also stimulate the regeneration of hepatocytes. Guided by the above mentioned parameters one can adequately use GCS and achieve the desired therapeutic effect with the least harmful effect on the body.

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