Evaluation of the effectiveness of information drugs in the inflammatory process in the experiment

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Inflammation is a pathogenic process that accompanies or underlies many diseases. The anti-inflammatory drugs available in the doctor's arsenal (hormonal, steroid and non-steroidal drugs; herbal drugs.) Are either not effective enough or cause a number of side effects. Exceeding therapeutic dosages leads to increased undesirable effects. The method of information transfer [1] can preserve the anti-inflammatory efficacy of the drug without increasing adverse reactions.

The aim of this study was to comparatively study the effectiveness of injectionforms of non-steroidal anti-inflammatory drug - sodium diclofenac in a therapeutic dosage [2]; information preparation (IP) obtained by transferring the information properties of the original preparation (diclofenac sodium, 3 ml) onto a secondary carrier - water for injection (2 ml); an enhanced information preparation (UIP) obtained by multiple rewriting of a therapeutic dose of diclofenac sodium per single dose of water for injection (0.05 ml).

Study design

The study was pilot and was carried out on a small number of white outbred male rats (20 animals) weighing 150–180 g. The animals were kept in standard conditions of a certified vivarium of the FBUZ "Center for Hygiene and Epidemiology in the Rostov Region".

The past few years have seen an increase in the number of studies aimed at assessing the pharmacological activity and efficacy of drugs under potentially reproducible conditions. This study was carried out on a model of subacute formalin inflammation [3] caused by the introduction of 0.1 ml of a 2% formalin aqueous solution under the aponeurosis of the ankle joint of the hind right paw of a rat. After 48 hours after the first injection of formalin, a second injection was carried out. The animals were divided into 4 groups: group 1 - animals of the control group; Group 2 - animals with the introduction of sodium diclofenac; Group 3 - animals with PI administration; Group 4 - animals with the introduction of UIP. The test substances were injected intramuscularly to animals at a dose of 0.05 ml (for greater accuracy of administration, insulin syringes with a volume of 0, 5 ml) 1 hour after the first injection of formalin, then after 24, 48, 72 hours, in total - 4 injections. Animals of the control group were injected with water for injection at a dose of 0.05 ml at the same time. The severity of edema was assessed by measuring the thickness of the paw with a caliper 1, 3, 6, 24, 48 hours after the first injection of formalin. Then the second injection of formalin was made and the paw thickness was measured after 49, 51, 54, 72, 96, 120 and 192 hours from the start of the study. To assess the effect of anti-inflammatory effects on the functional state of the animal organism, leukocyte formulas of rat blood were tested. The functional state of the body is associated with the development of general nonspecific adaptive reactions: stress reactions (Str) G. Selye [4] and anti-stress reactions of training (Tr) and activation [5]. Based on the indicators of the leukocyte formula, the level of intoxication was assessed [6], the adaptive reactions corresponding to the functioning of each animal were tested. Blood for analysis was taken from the femoral vein of rats at the following times: 1 - before the introduction of formalin (background); 2 - one day (24 hours) after the first injection of formalin; 3 - two days after the second injection of formalin (96 hours from the start of the study), that is, one day after the last of the four anti-inflammatory effects; the end of the experiment (192 hours from the beginning of the experiment and 120 hours after the end of anti-inflammatory effects). 3 - two days after the second injection of formalin (96 hours from the start of the study), that is, one day after the last of the four anti-inflammatory effects; the end of the experiment (192 hours from the beginning of the experiment and 120 hours after the end of anti-inflammatory effects). 3 - two days after the second injection of formalin (96 hours from the start of the study), that is, one day after the last of the four anti-inflammatory effects; the end of the experiment (192 hours from the beginning of the experiment and 120 hours after the end of anti-inflammatory effects).

Results and discussion

The greatest severity of edema in the control group was observed 6 hours after the first injection of formalin, was retained for 24 hours, increasing by 48 hours. Then, after the second injection

formalin, there was some inhibition of the increase in edema and again an increase in edema until the end of the study. In the groups with the introduction of diclofenac sodium and information drugs after 24 hours and up to 48 hours, the edema stabilized, and the least edema was observed in animals that received UIP. After the second injection of formalin (48 hours) and after the end of anti-inflammatory effects (72 hours) by 96 hours from the start of the study, an increase in edema of varying severity was observed in all experimental groups. At the end of the study, the smallest edema was observed in the animals of the group with the introduction of an enhanced information drug.

The severity of the increase in ankle edema was calculated by the formula (2), where: P - the increase in edema in%; O - the amount of edema after the introduction of formalin; And - the size of the paw before the introduction of formalin.

P = ((O - I) / I) x 100%.

The anti-inflammatory efficacy of the effects was assessed in% according to the degree of inhibition of the edematous reaction in comparison with the control (Table 1 and Table 2) according to the formula:
100 % - (O - I) / And (O): (O - I) / And (k) x 100%, k - control group; o - an experienced group.

Table 1

The severity of the increase in edema in% and the effectiveness of anti-inflammatory effects in% in relation to control after the first injection of formalin

Groups	Edema in% 6 hours	Effective rate in%	Edema in% 24 hours	Effective rate in%	Edema in% 48 hours	Effective rate in%
Control	71.4		71.4		85.7	
Diclofenac	42.8	40.1	57.1	20.0	57.1	33.4
SP	28.6	59.9	28.6	59.9	28.6	66.6
UIP	42.8	40.1	14.2	80.1	14.2	83.3

As you can see from the table. 1, the anti-inflammatory efficacy of information drugs was 2 or more times higher than the efficacy of sodium diclofenac.

table 2

The severity of the increase in edema in% and the effectiveness of anti-inflammatory effects in% in relation to the control after the second injection of formalin

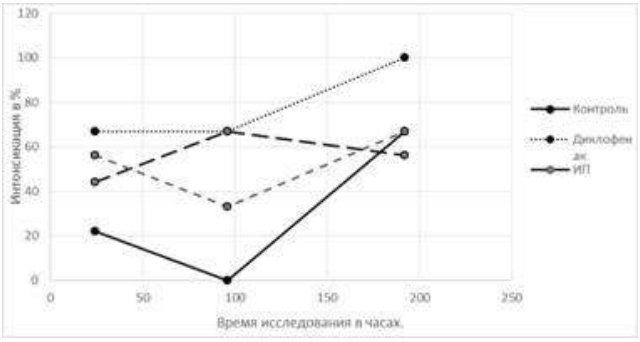
Groups	Edema in%, 96 hours	Efficiency in%	Edema in%, 192 hours	Efficiency in%
Control	85.7		100	
Diclofenac	71.4	16.7	100	0
SP	57.1	33.4	100	0
UIP	42.8	50.1	71.4	28.6

By the end of the study (192 hours from the start of the study and 120 hours after the end of the exposure), the severity of edema in the control group, experimental groups 1 and 2 - 100%. In the group of animals that were injected with the enhanced information drug, even after the end of the exposure, the severity of edema was less - 71.4% (Table 2). Only this group showed anti-inflammatory efficacy - 28.6%.

Thus, in the model of subacute formalin inflammation, a greater anti-inflammatory efficacy of information drugs with a more pronounced effect of the enhanced drug (UIP) was shown in comparison with diclofenac sodium.

According to the leukocyte formulas of the blood of animals, intoxication was assessed in experimental animals in the process of developing inflammation. Were used cell tests of reactivity and intoxication [6]: the shift index of blood leukocytes (ISLK) according to Yabluchansky; lymphocytic index of intoxication (LI) according to Kapitanenko and Dochkin; lymphocytic index of intoxication (LII) according to Kalf-Kalif and others. Results of counting the blood of animals of each of the groups

in all three tests, those who did not enter the normal zone (intoxication) were estimated as a percentage and presented graphically (Fig. 1).

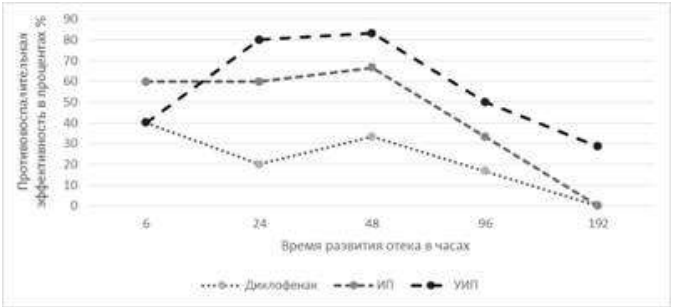


Rice. 1. Change in intoxication (in%) in the control, in the group with the introduction of sodium diclofenac, in the groupwith the introduction of IP and in the group with the introduction of UIP

As can be seen from the graph, the greatest intoxication was manifested in the group with the introduction of sodium diclofenac. Intoxication was lower in both groups with the introduction of information drugs.

According to the leukocyte blood formulas for each animal, the adaptive reactions developing during the study were determined. Before the start of the experiment (background), most of the animals demonstrated physiological adaptive responses: training response (Tr), activation response (Act), and increased activation response (PAD). During the study physiological adaptive responses were tested: in the control group in 66.7% (stress response was tested in 33.3%); in the group with the introduction of diclofenac in 73.8% (in 22.2%, the reactivation reaction - PeA was tested). In both groups with the introduction of information drugs, physiological adaptive responses were 100%. The severity of tension elements in the tested blood preparations in terms of the development of inflammation in each of the groups was different.

The harmony of developing adaptive reactions was assessed in points, according to the number of stress elements in each of the groups according to the timing of blood testing. A point assessment of the tension of developing adaptive reactions demonstrates an increase in the tension of adaptation of varying severity in all experimental groups and a certain decline by the end of the study. The greatest severity of this increase is demonstrated in animals of the control group, the least in animals from the group with the introduction of PI. At the end of the study, the tension of adaptation was least expressed in the groups with the introduction of information drugs: in the group with the introduction of PI (2 points) and slightly higher in the group with the introduction of UIP (4 points) (control, diclofenac –5 points). In the group with the introduction of PI, the tension of developing adaptive reactions throughout the study is less, than in the diclofenac sodium group. Figure 2 illustrates the anti-inflammatory efficacy of the enhanced information drug.



Rice. 2. Anti-inflammatory efficacy of diclofenac sodium, PI information drug , enhanced information preparation UIP

conclusions

Thus, it was shown on the model of subacute formalin inflammation that

the use of an information drug (IP) and an enhanced drug (UIP) has a more pronounced anti-inflammatory effect compared to diclofenac sodium with a reduced manifestation of side reactions. The manifestations of intoxication, both with the use of PI and with the use of UIP, were less than with the use of diclofenac sodium. Throughout the study, the animals of these groups developed only anti-stress adaptive responses of training and activation with less pronounced elements of tension. The anti-inflammatory response under the influence of PI and UIP occurred in the zone of the physiological norm.

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