Study of the effect of herbal medicines on the level rat blood urea in acute cold injury

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Cold injury is a severe injury and is currently considered one of the important causes leading to permanent disability of the injured [11, 17]. The study of the pathogenesis and effective methods of treatment and prevention of cold injury is important for improving the health of the population living not only in the northern regions of Russia, but also in milder climatic zones. Even in Moscow in the winter months, victims with cryoinjuries account for 20–25% of the total number of patients in emergency departments [12]. At the same time, up to 90% of frostbite occurs in a state of alcoholic intoxication [3, 4, 7].

Despite the large number of studies devoted to the study of drugs that increase "resistance" to cold, the treatment of frostbite is still a very difficult task. As a rule, drugs are used as freezoprotectors that affect the main links in the pathogenesis of frostbite with anti-inflammatory, antipyretic and analgesic effects (hormonal drugs, cytostatics, non-steroidal anti-inflammatory drugs, etc.). However, synthetic drugs are characterized by a number of disadvantages limiting their use, which include inhibition of the proliferation of lymphoid cells, the appearance of erosive and ulcerative lesions of the mucous membranes of the gastrointestinal tract, nephrotoxic and hepatotoxic effects. Therefore, based on the experience of traditional medicine, we proposed a recipe for fees,

Rationale for the choice of the research marker.notions, tBy mostcomplete pathogenesis of frostbite neurohumoral theory. The trigger mechanism inreflects development of frostbite is vascular spasm, which occurs as a result of activation of the sympathetic-adrenal system and inhibition of the anticoagulant system of the blood [7]. These changes can manifest themselves in the form of lesions, both local and systemic. Moreover, one of the systems reflecting deep physiological and biochemical changes in homeostasis under the influence of unfavorable environmental factors is blood [1, 14, 18].

Since the main pathogenetic processes in tissues develop during their external warming, when, along with the lack of adequate blood supply, there is an increased demand for oxygen and necrobiotic changes and tissue death occur. This pathology indicates a general toxemic reaction and changes in biochemical parameters [5]. It is known that

in the regulation of proteolysis, especially in the processes of adaptation to unfavorable environmental conditions, in particular to cold, along with other biological factors, an important role is assigned to urea [2, 13].

The analysis of our earlier results revealed a sharp increase in the level of urea in the blood serum of rats during frostbite. The maximum (3-fold in relation to the standard indicators) content of urea was recorded in samples taken from animals on the 3rd-6th day of the experiment.

The aim of this study was to study the effectiveness of 2 new herbal medicines (collections) with low toxicity and economic availability, on the model of acute cold injury. In this case, the level of urea in the blood serum of rats with frostbite was chosen as a criterion for their effectiveness.

Materials and methods. The experiments were carried out on conventional outbredwhite rats, mainly males weighing 160–180 g. The animals were on the usual diet. Acute cold injury was simulated by applying a jet of chloroethyl (-30 ° C) to the epilated skin of the rat's back, limited by a stencil with a diameter of 20 mm.

Two medicinal preparations were used as medicinal preparations, developed jointly by the staff of the Department of Pharmacology of the Northern State Medical University and the Institute of Homeopathy and Naturotherapy of the FNCE CTMDL. The preparations included only official plant raw materials [8]. The “core” of collection No. 1 consisted of birch leaves (Folia Betulae) and oregano herb (Herba Origani vulgaris), and collection No. 2 consisted of St. John's wort (Herba Hyperici) and yarrow grass (Herba Achilleae millefolii). Water extracts (10% infusions) from the collections were prepared according to the method of the State Fund of the XI edition [9]. The infusions were administered per os at a daily dose of 7.6 g per 1 kg of body weight of the rat in terms of dry weight of the collection. The share of 1 part of the plant was 800 mg / kg.

All animals were divided into 3 groups In 1 control (31 animals) rats were exposed only to the cold factor without the use of drugs. Animals of experimental groups 2 and 3, 100 rats in each, were injected orally with infusions of the fees. The rats of the 2nd group were exposed to the action of the cold factor against the background of the introduction of the plant harvest No. 1. The animals of this group were subdivided into three subgroups. In the first subgroup, the infusion from the collectionNo. 1 was injected for 3 days before frostbite (the so-called prophylactic scheme), in the second collection was injected according to the so-called. the combined scheme (both before and after frostbite). In the third subgroup, the infusion was administered only after frostbite (the so-called treatment regimen). The animals of the 3rd group were injected with collection No. 2 according to the scheme described above.

Cold injury was inflicted on the day designated in the diagram as "0" and was observed over the next 12 days. As markers of the effectiveness of our proposed collections, both in the control and in the experimental groups, the urea content in the blood serum of rats was used, which was determined according to standard methods on the 3rd, 6th, 9th and 12th days of the post-cold period, after decapitation of animals using a gentle technique [10].

Statistical processing of the results was carried out using the Statistica 6.0, SPSS 11.5 and Sigma Plot 8.0 packages. To assess the normal distribution, the Kolmogorov-Smirnov test was used. To assess the equality of variances, the Levene test was used. To study the differences between the groups, we used the method of one-way analysis of variance using the Tukey's test of plausibly significant differences [6, 16]. For a posteriori pairwise comparisons with equal variances and Tamhan's T2 test [15] with unequal variances. Differences were considered statistically significant at $p < 0.05$.

Research results. Of the total number of animalsOf the 1st (control) group, in which it was possible to induce frostbite of the II-III degree, 12 rats died (39% of the initial number of animals in the group). Death was observed throughout the experiment, but most of the animals died in the early post-cold period. The surviving rats were characterized by lethargy, decreased appetite, and a depressed reaction to external stimuli. The urea content progressively increased from 3.937 ± 0.860 mmol / L (initial values) to 8.994 ± 1.140 mmol / L (Fig. 1). The maximum amount of urea was determined on the 6th day of the experiment, further its level decreased, however, even on the last day (on the 12th day), the urea content in the blood of experimental rats was almost 2 times higher than in intact animals.

Experiments carried out in series with the introduction of infusions from the studied collections, showed a high degree of survival of the experimental animals. In each series, 1–2 rats died (ie, only 1–2% of the initial number of animals in the corresponding group, versus 39% in the control group). The surviving animals were distinguished by their activity and good appetite.

In the second series of studies (collection No. 1), a statistically significant decrease in the level of urea was observed for all administration regimens, approximately 2 times, compared with the control group (Fig. 1). With the prophylactic administration of the infusion, the urea level was 4.838 ± 0.595 mmol / L ($p < 0.001$), when using the treatment regimen it was 5.081 ± 0.255 mmol / L ($p < 0.001$), and with the combined administration - 4.395 ± 0.593 mmol / L ($p < 0.001$). In the subsequent period of observation on the 6th; On the 9th and 12th day, the general trend towards a decrease in the level of urea in the blood remained, reaching the initial value. The best results were obtained in animals to which the infusion was administered according to a combined scheme (before and after frostbite) or only preventively - before cold injury.

When the animals were administered infusion from collection No. 2, the level of urea in the blood of rats was statistically significantly lower than in the control group (Fig. 1). When using the prophylactic regimen, the urea content decreased by 53%, the combined route of administration - by 62%, and with the therapeutic administration, it decreased by 48.5% compared to the control values.

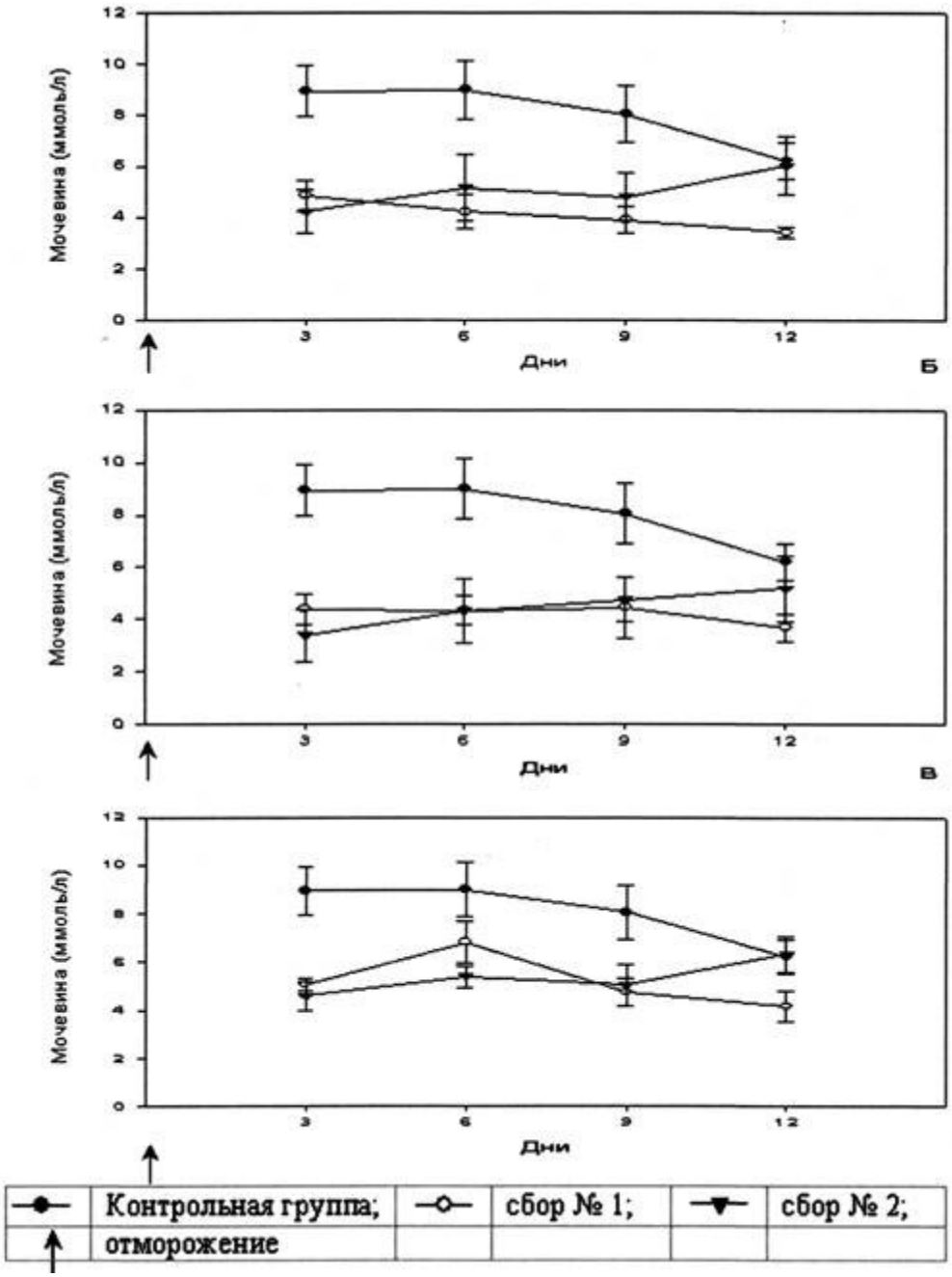
However, when using collection No. 2, the level of urea in the blood in the subsequent periods began to increase and its value on the 12th day was 6.035 ± 1.128 mmol / L for rats with preventive therapy, 5.173 ± 1.258 mmol / L with the combined method of administration and 6.317 ± 0.710 mmol / L with the treatment regimen, which did not have statistically significant differences from the control

group.

The discussion of the results. The studies carried out made it possible to establishthat the introduction of 10% infusion of collection No. 1 to animals led to a decrease in the level of urea already on the 3rd day of the post-cold period with any regimen of use. The urea content also significantly differed from the control values on the 6th, 9th and 12th day of the experiment.

Probably, these results are explained by the presence in the composition of the “core” of the collection: birch leaves, which have anti-inflammatory, antiseptic and wound-healing effects, and oregano herb, which has anti-inflammatory, analgesic, diuretic, antiseptic, sedative and antispasmodic properties. In the same collection there is licorice root, which activates the activity of the adrenal cortex and stimulates the formation and release of glucocorticoids into the blood, which have a pronounced anti-inflammatory effect.

With the introduction of 10% infusion of collection No. 2 to animals of the 3rd group, the levels of blood urea, determined on the 3rd day of the post-cold period, had statistically significant differences from the control values.



Rice. 1. Changes in the level of blood urea in rats (M± s) in experiments with prophylactic (A), combined (B) and therapeutic (C) administration of charges No. 1 and No. 2 in comparison with the control group.

The maximum decrease in this indicator (by 62% compared to the control) was recorded in the group of rats that received the infusion according to the combined scheme. Similar data were obtained in the other two subgroups of animals, however, the degree of their difference with the control values was less pronounced. Further, in blood samples taken on the 6th; On the 9th and 12th day of the experiment, the tendency for a decrease in the urea content persisted in rats of all

three subgroups, however, on the last day of observation, these indicators did not have statistically significant differences from the control group, although they remained significantly higher than the level in intact animals. The data obtained were convincing evidence of the possibility of normalization of the altered urea marker in cold injury by prescribing the infusion of collection No. 2. The recorded differences in the efficiency of the collection, assessed by the normalization of the level of urea in the blood of rats, are probably explained by the pharmacological properties of a number of ingredients in the collection. In particular, weaker manifestations of anti-inflammatory action in collection No. 2, compared with collection No. 1.

However, this does not exclude the need for further study of the effectiveness of both collections in terms of their influence on other indicators of homeostasis.

conclusions

1. A study of the effectiveness of 2 new fees, compiled with taking into account the experience of traditional medicine in Russia based on birch leaves, oregano herb, St. John's wort, yarrow herb, in the treatment of frostbite.

2. When using any of the used schemes for introducing the collection infusion No. 2, the urea content in rats, determined on the 12th day of the post-cold period, did not have statistically significant differences with the data of the control group, but was higher than the values in intact animals.

3. Collection No. 2, introduced to the animals by the combined method, caused the maximum (by 62%), in comparison with the control values, decrease in the level of urea on the 3rd day of the post-cold period.

4. Collection No. 1, introduced in the periods before, after frostbite, as well as before and and after it, contributed to the normalization of the level of urea in the blood of experimental animals to the level of intact animals with all regimens of use in comparison with the control group.

5. In connection with the cold injury established on the used model different effectiveness of the use of fees for frostbite, it is advisable to continue the study of both prescriptions of fees in terms of their influence on other indicators of homeostasis.

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