PROPHYLACTIC EFFECTS OF ATROPINE SULFATE AND DICLOFENAC SODIUM ON THE COURSE OF ASEPTIC INFLAMMATION INDUCED BY DEXTRAN AND CORRAGEENIN

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INTRODUCTION

Most human diseases are caused by an inflammatory process under the influence of an etiological factor. At the same time, there are a number of diseases, including rheumatological diseases, in the pathogenesis of which the inflammatory process lies. Nonsteroidal anti-inflammatory drugs (NSAIDs), which have fewer side effects than steroidal anti-inflammatory drugs, are widely used in the pharmacological correction of the inflammatory process.

NYaQV is the most common group of drugs, which are widely used to reduce inflammation, body temperature or relieve pain (E.L. Nasonov, 2005; A.L. Khokhlov, 2005; I.A. Zupanets, V.A. Tulyakov, 2005). In a number of countries of the world, 10-20% of the population over 65 years of age receives NCDs (Moore N., 2003). NYaQV is widely used in the treatment of inflammatory diseases of joints, skeletal muscles, headache and toothache. In the USA, 13 million citizens receive NYaQV per day (V. Fisenko, 2001). 20% of the population of our planet regularly take NYaQV; if 40 million people take some NYaQV in one day, a third of them accept taking this tool as they know (N.I. shvets, T.M. Bentsa., 2002; A.P. Viktorov., 2003). However, taking NYaQV is characterized by a high rate of side effects, including NYaQV-gastropathies or gastrointestinal toxicity from the gastrointestinal tract (gastroduodenal erosions, peptic ulcers of the stomach and duodenum and their other complications - bleeding, perforation, obstruction of the gastric outlet, death). According to literature data, they belong to common iatrogenic pathologies in developed countries and are considered one of the urgent problems of the healthcare system (V. Fisenko, 2001; I.R. Mavlyanov, 2002; N.I. Shvets, T.M. Bentsa, 2004). . A number of efforts are being made to prevent severe side effects of NSAIDs: they are used in combination with sucralfate, N2-histamine receptor inhibitors, prostaglandin analogs, and proton pump blockers. In such combinations, the gastrointestinal tract activity of NSAIDs is less disturbed, but the negative effect on the stomach remains high when NSAIDs are used

together with misoprostol (a synthetic analogue of PGE1). Misoprostol, in particular, increases the cost of NSAIDS, as diarrhea caused by its use greatly limits the use of this combination (diclofenac + mizorostol). New drug forms (intestinally soluble tablets, suppositories) could not eliminate the negative effects of NSAIDs on the gastrointestinal tract (V. Fisenko, 2001; A.P. Viktorov, 2003).

The purpose of the study. Study of the prophylactic effect of atropine sulfate and diclofenac sodium on the course of aseptic inflammation induced by dextran and corrageenin.

Materials and Methods. To perform the experimental part of our scientific work, we used 120 purebred male rats in normal vivarium conditions. Test drugs were administered in the following doses; Atropine sulfate 0.5 mg/kg, 1 mg/kg intragastrically through a metal probe, and diclofenac sodium (1 mg/kg), a currently widely used NYaKV drug, was used as a comparator. The anti-inflammatory effect of the drug was evaluated by the differences in the paws of the rats in the control and experimental groups.

It was found that atropine sulfate has stronger anti-inflammatory activity when it is administered by the same method. In order to determine the anti-inflammatory activity of an orally administered drug, a variety of phlogogenic agents commonly used to induce arthritis were challenged at the following concentrations; dextran (6%), formalin (2%) solutions were injected under the paw skin of the hind paw of animals in a volume of 0.1ml/kg. Test preparations were administered to animals 1 hour before administration of phlogogenic agents. The size of the paw was measured using a water plethysmometer (oncometric method) before the introduction of the phlogagen agent and during a specified hour, and the results were recorded.

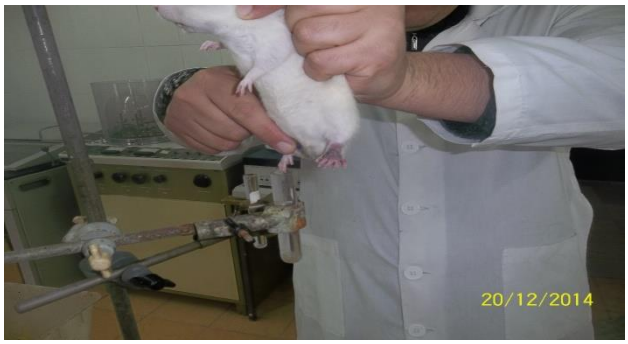
When determining the anti-inflammatory activity of the drug (atropine sulfate), the ratio of the size of the paw before the experiment to the size of the paw during the experiment was determined using mathematical calculations. Rheumatoid joint injury is based on the inflammatory process. To eliminate it, anti-inflammatory drugs are used. Taking this situation into account, an adjuvant arthritis model in experimental animals was called.

"Cotton pellet" method recommended by Meijer et al. was used to study the effect of drugs on the proliferative phase of inflammation. The results of the experiment conducted using the "Cotton pellet" method determined the anti-inflammatory activity of the investigated drug.

A number of researchers choose formalin as a phlogogenic agent in most cases, because the inflammatory process induced by formalin is similar to the

inflammatory process in humans. Therefore, the formalin tumor model is used to study the anti-inflammatory activity of drugs.

In our studies, we injected 0.2 ml of 1% formalin subplantarly into the rat and measured the initial volume of the aqueous plethysmometer (oncometric) formalin-injected paw and the volumes 3.6 and 24 hours after infection.



Picture. . Determining the paw size of rats with a plethysmometer

The anti-inflammatory activity of the drug was evaluated by the difference between paws before the experiment and at the time when maximum swelling developed.

Animals were divided into 4 groups to study the anti-inflammatory activity of the drug atropine sulfate. Based on the criteria of comparison, prophylactic administration of atropine sulfate and diclofenac to animals was envisaged. 1 group - atropine sulfate was administered orally in a dose of 0.5 mg/kg, group 2 - in a dose of 1 mg/kg intraperitoneally. Group 3 - diclofenac (10 mg/kg) was administered orally. Group 4 is the control group, in which the rats were given distilled water in the above order.

Picture. Techniques for administration of test drugs to experimental animals

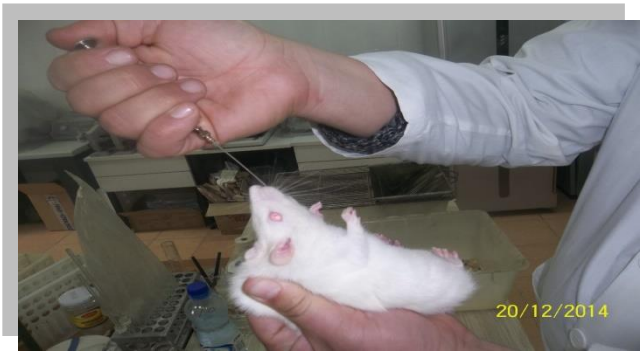
In the next part of our experiments, the experimental animals were divided into 3 groups to study the efficacy of diclofenac and atropine sulfate drugs. In order to study the prophylactic effect of atropine sulfate, 1 group of animals was given intraperitoneally 1.5-2 hours before the onset of inflammation, and 2 groups were given diclofenac intragastrically at a dose of 10 mg/kg. administered 1 hour before the onset of inflammation. Group 3 is the control group, in which the rats were given distilled water in the above order.

The NQF of the drug was calculated according to the following formula:

$$QA = \frac{\text{Control-Experience}}{\text{Control}} * 100$$

To study the effect of atropine sulfate and diclofenac on the proliferative stage of inflammation, the "cotton pellet" method proposed by Meijer was used.

Rats were given light ether anesthesia one hour before, and sterile cotton swabs (10ml/kg) were implanted between two scrotums. Prophylactically, the study drug was administered every day for 7 days. On the eighth day, the rats were decapitated using light ether narcosis, cotton balls were separated together with granulation tissues, and after their weight was measured, they were placed in a thermostat at a temperature of 70 °C. It was dried to constant weight. The difference between the dry pellet weight and the wet pellet weight indicates the exudative phase of inflammation, and the difference between the pellet weight and the resulting granulation tissue indicates the proleferative phase. All experiments were carried out in accordance with the European convention on the use of experimental animals. (Strasburg 1986) All the data obtained from our experiment were calculated using the statistical Windows package



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For this purpose, 5 mg of sterile cotton balls were implanted into the subcutaneous tissue of the scapula of rats 1 hour after the administration of the drugs under the influence of light ether anesthesia. Atropine sulfate and diclofenac were administered daily for 7 days. On the 8th day, experimental animals were killed by decapitation, cotton balls covered with granulation-fibrous tissue were taken, their wet weight was measured, and then dried at a temperature of 70 0C, and its dry weight was measured. The resulting granulation tissue mass was determined by the difference in the weight of the dried granuloma and the implanted cotton ball.

The obtained data were expressed in percentages, and the arithmetic mean value and its standard error were calculated using the method of variational statistics.

RESULTS AND ITS DISCUSSION

Unlike other phlogogenic agents, dextran affects mast cells when applied locally, and this process is manifested by the release of inflammatory mediators - histamine and serotonin.

When studying the effects of atropine sulfate and diclofenac on dextran inflammation in experimental animals, it was found that the phlogogenic agent showed its maximum effect 1 hour after exposure to the damaging agent.

In addition to the increase in the size of the rat's paw in the animals injected with atropine sulfate and diclofenac, its appearance was almost the same in both groups of animals. When the anti-inflammatory effect of diclofenac was studied, after 1 hour the paw volume of rats was 1.2 ml, which was 2 times larger than the initial results, and this trend was maintained during all periods of observation.

Figure 3. Effects of atropine sulfate and diclofenac on dextran-induced inflammation

The anti-inflammatory effect of atropine sulfate is evident, in which 1.17 ml in 1 hour of observation, 0.9 ml in 2 hours, 0.8 ml in 3 hours, and 0.0.76 ml after 4 hours were recorded, and this the results are 2.2, respectively, compared to the initial results; 1.55; 1.38 and 1.25 times higher means.

2 tables

Anti-inflammatory effects of atropine sulfate and diclofenac induced by dextran

Mean volume of the paw of the drug, ml Increase in the volume of the paw compared to the initial results, %

Normal ml % 3 hours after administration of Dextran

Control 0.54+0.02 1.21+0.09* 0.67 124.1 0

Diclofenac 0.59+0.04 0.93+0.05* 0.34 57.6 97.1

Atropine sulfate 0.55+0.03 0.81+0.04* 0.26 47.3 61.2

* - P<0.05 reliable difference compared to standard values

As a result of the experiments, it became clear that both the used drugs and dextran slowed down the course of arthritis. 3 hours after the administration of dextran, the average volume of the paw in the animals of the control group was 1.21 + 0.09 ml, in the group treated with diclofenac at a dose of 10 mg/kg it was 0.93 + 0.05 ml, and in the case of atropine sulfate - 0.81 + 0. It was equal to .04 ml. These results were found to be 55.3% higher than the norm in the control group, 36.6% in the diclofenac group, and 32.1% in the atropine sulfate group. Compared to the initial results, the growth index of the paw of rats was 124.1% in the control group, 57.6% in the diclofenac group, and 47.3% in the group of animals treated with atropine sulfate. The anti-inflammatory activity of diclofenac and atropine sulfate was 97.1% and 61.2%, respectively.

By comparing the obtained results, it can be concluded that although atropine sulfate has a significant anti-inflammatory effect in dextran arthritis (62.2%), it is weaker than the anti-inflammatory effect of diclofenac (97.1%), and it was found that the AQF of diclofenac is 1.5 times higher than that of atropine sulfate. .

The conclusion. This effect of diclofenac may be due to its stabilization of the membranes of lysosomal membranes, reducing its permeability (***). As a result, various lysosomal hydrolases are reduced in the intercellular space. In addition, this is related to the effect of the drug on mediator processes, that is, it is associated with a decrease in capillary permeability and a decrease in the migration of leukocytes to the inflammatory site.

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