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PHARMACOKINETICS OF ANTIBIOTICS IN EXPERIMENTAL GUNSHOT WOUNDS

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ABSTRACT:

Experimental studies on the pharmacokinetics of gentamicin were performed on 40 rabbits with various methods of injection after the infliction of gunshot wounds on extremities. The results showed that the method of lymphotropic antibiotic therapy provides a more stable and long-term saturation of blood. The highest and the longest retaining concentration of gentamicin in the lymph nodes and soft tissue of gunshot wounds is reached at lymphotropic method of injection.

KEYWORDS: gunshot wound, lymphatic antibiotic therapy, antibiotics pharmacokinetics.

INTRODUCTION:

The use of firearms possessing high kinetic energy has led to an increase in the number of serious injuries that significantly damage the soft tissues, but the problem of prevention and treatment of purulent complications of gunshot wounds remains topical. There is a lot of experience in the effective application of lymphotropic therapy (LT) in the treatment of surgical infections, but there are only a few studies on the lymphotropic antibiotic treatment for gunshot wounds and on its pharmacokinetics .

RESEARCH OBJECTIVE:

Pilot study of the pharmacokinetics of gentamicin in lymphotropic therapy (LT) with regional lymphatic stimulation (RLS) compared to conventional injection methods

RESEARCH MATERIALS AND METHODS:

Experimental studies were conducted on 40 rabbits of both sexes with a weight of 5-6 kg. An experimental model of gunshot wounds was used. Fifteen minutes before the injury all the animals from experimental and control groups were under kalipsol anesthesia, after which they were fixed on special plates. Standard gunshot wound of the soil tissues was applied to the region of the middle third of the right femur of the rabbit. For the study of pharmacokinetics we used gentamicin 1 mg/kg, which corresponds to the average therapeutic dose for an adult.

Regional lymphatic therapy (RLT) was carried out by the following method. Under the skin of the calf on the border of the lower and middle thirds of the rear surface the

lydasa (Hyaluronidasum) solution was injected in the amount of 16 units. After 4-5 minutes, without removing the needle, an antibiotic (gentamicin at a dose of 1 mg/kg) was injected. In the same section heparin was injected at a dose of 70 units/kg. Lymphotropic infusion of antibiotics with RLS was performed 1 time per day.

The experimental animals were divided into 4 groups. In (the first group of experiments gentamicin was injected lymphotropically (LT) to 10 rabbits, as in the method described above.

In the second group (control), 10 rabbits were injected subcutaneously (SC) with gentamicin without using lymph stimulators. In the third group (10 rabbits), gentamicin was injected intramuscularly (IM) in the thigh area.

In the fourth group of experiments (10 rabbits), gentamicin was infused into a peripheral vein - intravenously (IV). To determine the concentration of antibiotic, the serum of blood in the amount of 1.4 ml was taken after 0.5, 1, 3, 6 and 24 hours after the injection of gentamicin. After 6 hours a part of the animals following the IM (5 rabbits), IV (5 rabbits), SC (5 rabbits) and LT (5 rabbits) infusions were deliberately withdrawn from the experiment by injection of high doses of kalipsol. Another part of the animals following the LT (5 rabbits) and then SC, IM, IV (5 rabbits in each series) infusion methods were pulled out from the experiment 24 hours after the injection of kalipsol. It allowed at a specified time to extract the inguinal lymph nodes and slices of soft tissues from a gunshot wound. Gentamicin in extracts of biological material was detected by high performance of liquid chromatography (HPLC) after prior receipt of phenyl derivative gentamicin using phenyl isothiocyanate - PhlTC (Sigma, USA).

RESEARCH RESULTS:

The analysis of the pharmacokinetics of gentamicin at various methods of injection shows that traditional methods reach the peak concentrations in the period of time equal to 0,5-1 hour. Then, the concentration quickly drops and within 6 hours after the injection, the drug levels in different animals range from "marks" of the antibiotic to 1,6 mcg/ml. Mean values of concentration did not reach therapeutic values. By the lymphotropic injection the highest concentration falls within the period of time of 1 hour, and this testifies to the relatively rapid penetration of the drug in high enough concentrations into the blood. After 6 hours the concentration of antibiotic in the blood by lymphotropic injection is 1.8-3.4 times higher than in the experiments with intramuscular, intravenous and subcutaneous injections of the drug. After 24 hours, with the traditional injections, gentamicin in the blood was not detected in any of the animals, whereas, lymphotropic injection created a concentration of gentamicin, similar to therapeutic value, an average of 1.07 + 0.23 mcg/ml. These concentrations are inhibitory to most microorganisms, which are most frequently encountered in surgical patients. Also, it should be noted that after a single lymphotropic injection of the drug in the medium therapeutic dose it creates subtherapeutic concentrations in the blood in 24 hours, given the possibility of lymphotropic antibiotic therapy once a day.

Comparing the contents of gentamicin in the inguinal lymph nodes and soft tissue gunshot wounds of extremities with various methods of application showed that 6 hours after the injection the largest concentration, corresponding to 1.44 + 0.64 mcg/g, in the inguinal lymph nodes was created by the

^mphotropic method. With intramuscular injection after 6 hours in the inguinal lymph nodes only "marks" of the antibiotic were noted. In soft tissue gunshot wounds 6 hours after the intramuscular and subcutaneous injection an antibiotic was either not detected or it was kept in small concentrations. By intravenous infusion the antibiotic concentrations in the soft tissues remained low (0.12 + 0.06). The lymphotropic method does not provide high concentrations in the soft tissues of the extremity. However, 24 hours after the lymphotropic injection gentamicin was still determined in the inguinal lymph nodes and soft tissues of gunshot wounds of extremities in concentrations of "marks" up to 0.87 mcg/g, whereas the traditional methods of drug were not detected in the study.

CONCLUSIONS:

1. Lymphotropic antibiotic therapy method, when used with the medium therapeutic dose of the antibiotic, injected one time, in comparison with traditional methods provides a more stable and long-term saturation of blood.
2. Comparatively high and continuously retaining concentrations of gentamicin in the lymph nodes are reached by lymphotropic injection. Injected this way an antibiotic is kept in the soft tissue gunshot wounds of extremities for a longer time than with traditional methods.

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