PHARMACOLOGY

THE ACTION OF SOME INDUSTRIAL POISONS ON THE MECHANISM OF TRANSMISSION OF THE NERVE IMPULSE IN THE SUPERIOR CERVICAL SYMPATHETIC GANGLION

COMMUNICATION I. ACUTE EXPERIMENTS WITH HYDROGEN SULFIDE, ETHYLENE AND PROPYLENE ON HEALTHY ANIMALS

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The industrial poisons hydrogen sulfide and the unsaturated hydrocarbons ethylene and propylene are gases with which workers in the oil industry often have to come in contact during the manufacture of gasoline. Much work has been done to study the action of hydrogen sulfide and the ethylene hydrocarbons on the activity of the heart, the blood, gastrointestinal tract, eyes, hearing and nervous system; the subject of the effect of hydrogen sulfide and unsaturated hydrocarbons on the synaptic transmission of the nerve impulse, and in particular in the sympathetic nervous system, has been neglected.

We decided to try to rectify this omission, using the method of perfusion of the superior cervical sympathetic ganglion, developed by Academician K. M. Bykov and A. M. Pavlova [1] and by A. V. Kibyakov [2], and repeatedly commended both in the USSR and abroad.

EXPERIMENTAL METHOD

Experiments were carried out on cats, since they have a well-developed nictitating membrane, the contraction of which may be recorded on the smoked surface of a kymograph with a slowly revolving drum. After dissection of the superior cervical sympathetic ganglion, usually under urethane anesthesia (1 g/kg body weight, intraperitoneally), and setting up the system of perfusion of the ganglion with Ringer-Locke solution, the contractions of the nictitating membrane of the cat were recorded in response to stimulation of the preganglionic fibers by the electric current. The strength of the stimulating current was always 20 mm above threshold. Next, hydrogen sulfide, in a dose of 2 ml of a concentration of 0.1-1.0 mg/ml of Ringer-Locke solution, was injected by means of a syringe into the carotid artery, which supplies the perfused ganglion, and the contractions of the muscle of the nictitating membrane were again recorded in response to electrical stimulation of the preganglionic fibers with a current of the same strength.

EXPERIMENTAL RESULTS

The experiments showed that hydrogen sulfide, in a concentration of 0.2-0.5 mg/ml Ringer-Locke solution, caused excitation of the ganglion cells, and this excitation was removed by atropine added to the perfusion solution in concentration of $1{:}10^{6}$.

In higher concentrations (0.6-1.0 mg/ml Ringer-Locke solution), on the other hand, hydrogen sulfide has a depressing action on the superior cervical sympathetic ganglion, which proceeds along the lines of a Vvedenskii parabiosis. This effect can be abolished by cocaine; furing perfusion of the superior cervical sympathetic gang - lion with Ringer-Locke solution containing cocaine in concentration of $1:10^6$ the phenomenon of depression no longer develops in response to hydrogen sulfide.

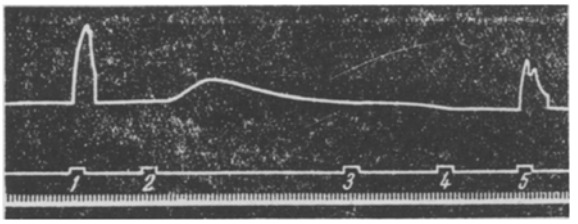

Fig. 1. The action of hydrogen sulfide on the humoral transmission of the nerve impulse in the superior cervical sympathetic ganglion.
Significance of the curves (from above down): contraction of the muscle of the nictitating membrane of the cat; stimulus marker and marker of injection of hydrogen sulfide and of "active perfusate" (1, 5 – response to electrical stimulation of the preganglionic fiber; 2, 4 – injection of 2.5 ml of "active perfusate" into the artery of the ganglion; 3 – injection into the artery of the ganglion of hydrogen sulfide in a concentration of 0.7 mg/ml Ringer-Locke solution, in a volume of 2 ml); time marker (5 seconds).

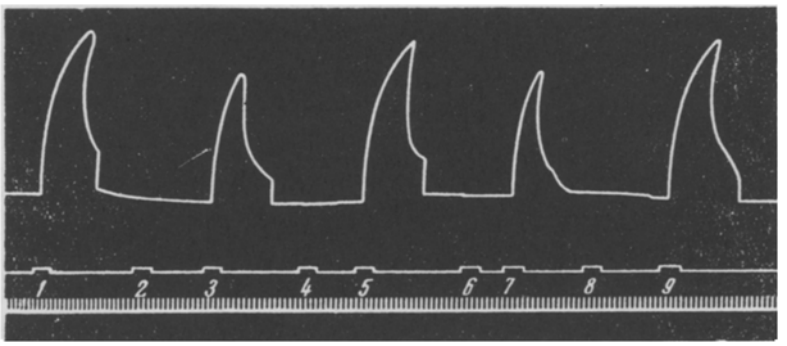

Fig. 2. Depressing action of hydrogen sulfide (concentration 0.8 mg/ml Ringer-Locke solution) on the superior cervical sympathetic ganglion and the restorative action of vitamins B_2 and C.
Significance of the curves (from above down): contraction of the muscle of the nictitating membrane of the cat; marker of stimulus and of injection of hydrogen sulfide and vitamins (1, 3, 5, 7, 9 – response to electrical stimulation of the preganglionic fiber; 2, 6 – injection of hydrogen sulfide into the artery of the ganglion; 4 – injection of vitamin B_2 in a dose of 2 ml of a concentration of 50 mg/100 ml Ringer-Locke solution; 8 – injection of vitamin C in a dose of 2 ml of a concentration of 50 mg/100 ml Ringer-Locke solution into the artery of the ganglion); time marker (5 seconds).

On the basis of these experiments we were able to state that hydrogen sulfide abolished primarily the humoral transmission of the nerve impulse, not the electrical (Fig. 1). If at first on the smoked surface of the kymograph drum are recorded the contractions of the nictitating membrane of the cat in response to electrical stimulation of the preganglionic fibers, and then in response to the injection of active perfusate * into the artery of the ganglion and we then inject into the artery of the ganglion hydrogen sulfide in a dose of 2 ml of a concentration of 0.7 mg per ml Ringer-Locke solution, then against the background of this poisoning of the ganglion, the contractions of the nictitating membrane of the cat from electrical stimulation of the preganglionic pathways occurs, although they are diminished, but the humoral transmission of the nerve impulse disappears completely.

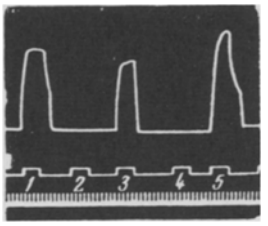

Fig. 3. The toxic action of propylene (concentration 0.4 mg/ml) and the restorative effect of vitamin B_6 on the superior cervical sympathetic ganglion. Significance of the curves (from above down): contraction of the muscle of nictitating membrane of the cat; marker of stimulus and of injection of propylene and vitamin B_6 (1, 3, 5 – response to electrical stimulation of the preganglionic fibers; 2 – injection of propylene into the artery of the ganglion; 4 – injection of vitamin B_6 in a dose of 2 ml of a concentration of 50 m/100 ml of Ringer-Locke solution); time marker (5 seconds).

A fact of great interest is the removal by vitamins B_2 and C of the depressing influence of hydrogen sulfide on the transmission of the nerve impulse in the superior cervical sympathetic ganglion. Vitamins B_2 and C not only abolish the toxic action, but if injected into the artery of the perfused ganglion before the action of hydrogen sulfide on it, in concentration of 0.6-1.0 mg/ml, they prevent the development of depression of the ganglion (Fig. 2).

In our later experiments to elucidate the action of unsaturated hydrocarbons on the synaptic transmission of the nerve impulse in the superior cervical sympathetic ganglion, we had the following aims:

1) To investigate what effect – depressing or exciting – was shown on the synaptic transmission of the nerve impulse in the superior cervical sympathetic ganglion by such products of oil refining as ethylene and propylene;

2) To ascertain precisely which form of transmission of the nerve impulse – humoral or electrical – was primarily affected; and

3) To select antagonists to neutralize the toxic action of the products of oil refining on the sympathetic nervous system.

Our experiments showed that ethylene injected into the artery supplying the ganglion in a concentration of 0.1 mg/ml Ringer-Locke solution and a dose of 2 ml, and propylene in a concentration of 0.4 mg/ml, have a slowly developing depressing action on the synapses of the sympathetic nervous system; under these circumstances propylene is more toxic than ethylene. Attention is drawn to the fact that the humoral transmission of excitation in the superior cervical sympathetic ganglion is suppressed primarly by these poisons as is also the case with hydrogen sulfide, and often it disappears completely, but the electrical conduction of the nerve impulse, although depressed, is nevertheless preserved (Fig. 3). During perfusion of the ganglion with Ringer-Locke solution containing cocaine in a concentration of $1:10^6$, this phenomenon of depression is absent. The disturbance of conduction of the nerve impulse through the synapse is also readily restored by injection of vitamins B_2, C and B_6 into the ganglion; vitamins B_1, PP and B_{12} do not possess this action.

In some experiments we found functional changes in the ganglion, which by their character were reminiscent of the equalizing and paradoxical stages of Vvedenskii.

* By active perfusate we imply the fluid collected from the internal vein of the sympathetic ganglion during stimulation of the preganglionic pathways by means of an electric current, and capable, on reinjection into the artery of the perfused ganglion, of causing contractions of the muscle of the nictitating membrane of the cat.

The excitant effect of hydrogen sulphide on the superior cervical sympathetic ganglion in cats may be removed by atropine, while the depressing one – by cocaine. Under the effect of hydrogen sulfide, ethylene and propylene the humoral transmission of the nerve impulse in the superior cervical sympathetic ganglion disappears earlier than the electric transmission. The functional changes produced as a result of the action of ethylene and propylene on the superior sympathetic ganglion are of the Vvedenskii parabiosis type. Vitamins B_6, B_2 and C remove the inhibitory effect of hydrogen sulfide, ethylene, and propylene on the superior cervical sympathetic ganglion of cats and render a protective effect. Vitamins B, PP, B_{12} lack such an effect. All experiments were conducted on healthy cats.

SUMMARY

Hydrogen sulfide has an exciting effect on the superior cervical sympathetic ganglion of cats in the concentration of from 0.2 to 0.5 mg/ml in Ringer-Locke solution and a depressive effect in the concentration of 0.6– 1.0 mg/ml in Ringer-Locke solution.

LITERATURE CITED

[1] K. M. Bykov and A. M. Pavlova, Collection Commemorating the 75th Birthday of I. P. Pavlov, 413-425, (Leningrad, 1924). [In Russian]

[2] A. V. Kibyakov, Kazansk. Med. Zhur., 5-6, 457-467 (1933).