EXPERIMENTAL DATA ON THE THERAPEUTIC EFFECT OF PARA-AMINO-SALICYLIC ACID (PAS)

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Although PAS is widely used for tubercular diseases, the mechanism of its effect has not been sufficiently studied. More particularly, the question of PAS's effect on the nervous system and the importance of this effect to the mechanism of the preparation's therapeutic action has only been touched upon. With this in mind, we decided to study the effect of PAS on the interoceptive reflexes.

In previous works conducted on healthy cats[6, 7], we established that PAS causes stimulation of the chemoreceptors by indirect contact with them. In the second phase of its action, the preparation causes a reversible functional interruption or a considerable decrease in chemoreceptor excitability. It was also established that PAS injected intramuscularly inhibits reflexes from the chemoreceptors, while increasing the reflexes from the mechanoreceptors in a majority of experiments.

In this work, we present results obtained in experiments studying the effect of PAS (0.25-1.0 per 1 kg of weight) on reflexes caused by stimulating the chemoreceptors of the small intestine, the receptors of the carotid sinus reflexogenic zone and the bladder mechanoreceptors in animals suffering from tuberculosis.

EXPERIMENTAL METHODS

A total of 19 animals were infected with an emulsion of bovine tuberculosis microbes (K-2 strain). The culture was injected into the femoral vein in a dose of 0.025-0.02 mg per 1 kg of weight.

The animals were used in the experiment 10-25 days after the infection, after which they were subjected to careful pathologico-anatomical examination. Tuberculosis was observed in all of the animals beginning the 14th day after infection, and becoming most strongly expressed on the 20th-25th day after infection.

The arterial pressure and respiratory reflexes from the chemoreceptors of the small intestine were examined under conditions of perfusion of the organ, which was isolated from circulation. We used acetylcholine in a concentration of $1 \times 10^{-4}$ (1 ml) or carbon dioxide as a stimulant. The reflexes from the carotid sinus reflexogenic zone were elicited by pressure on the common carotid artery for a period of 15 seconds, and the reflexes from the bladder mechanoreceptor, by air expansion of the bladder walls with a pressure of 80-100 mm of mercury.

EXPERIMENTAL RESULTS

In the majority of experiments conducted, PAS caused the reflexes from the chemoreceptors of the small intestine to decrease by 25-75%. In several experiments, the reflexes from the chemoreceptors became inhibited as soon as 15-20 minutes after the PAS injection (Fig. 1).
The reflexes from the receptors of the carotid sinus reflexogenic zone were completely inhibited. In this series of experiments, as opposed to the experiments on healthy animals, the reflexes from the bladder mechanoreceptors were also inhibited. Only in 3 out of 11 experiments were the reflexes observed to increase. In 8 experiments, the reflexes decreased (Fig. 2), and in 2 experiments, the reflex remained practically the same. The PAS injection also inhibited the respiratory reflexes in the majority of experiments.

Fig. 1. Decrease in reflexes from the chemoreceptors of the small intestine in an animal with tuberculosis after intramuscular injection of PAS (0.5 g per 1 kg of weight).

a, b) Initial reflexes; c, d, e) reflexes after PAS injection. Curves from top to bottom signify: respiration, blood pressure, indication of stimulation, indication of time (in 5 second marks).

Fig. 2. Decrease in reflexes from bladder mechanoreceptors in an animal with tuberculosis after PAS injection. PAS injected at 12:32 PM.

a, b) Initial reflexes; c, d, e) reflexes after PAS injection. Curves mean the same as in Fig. 1.

Having established that PAS, parenterally injected, has a primarily inhibitory effect both in healthy and tubercular animals on the reflexes from the chemoreceptors, we went on to determine what effect PAS had when inadequate stimulants, causing pathological reactions, were used. We used post-transfusion shock for this study.

It has recently been established (2, 9 and others) that the reflexes from the vascular chemoreceptors, which occur due to the stimulation of these chemoreceptors by heterogeneous blood and by the secondary products resulting from the reaction of the host's blood with the transfused blood, play an important part in the development mechanism of post-transfusion shock.

We caused shock to develop by infusing 10 ml of preserved donor's blood into a femoral vein. The experiments were done on 18 cats. The animals were matched in pairs according to sex and weight and then separated into a control and an experimental group. The animals were intramuscularly injected with PAS in a dose of 0.5-1 g per 1 kg of animal weight 45 minutes to 1 hour, 25 minutes before the experiment.

In all of the control experiments, the infusion of 10 ml of preserved blood into the femoral vein caused