PHARMACOLOGY

THE GANGLIOPLEGIC PROPERTIES OF AMINAZINE (LARGACTIL) AND MEPAZINE (PACATAL)

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In studying the pharmacological properties of largactil (aminazine) Laborit and his co-workers [12, 13] came to the conclusion that this compound possesses gangliolytic properties. Many other authors [1, 3, 4, 5, 9, 17] hold the same viewpoint. At the same time there appeared in the literature reports denial of the ability of largactil to depress the transmission of stimulation in the autonomic ganglia [6, 7, 8, 16]. General opinion holds this question still open to debate [10, 11, 14, 15].

The aim of the present research is to clarify whether largactil influences the transmission of stimulation in the superior cervical ganglion of the cat.

EXPERIMENTAL METHODS

In experiments on decerebrated cats simultaneous recording was maintained of the biopotentials of the postganglionic fibers and the contractions of the nictitating membrane. The preganglionic fibers were irritated with rectangular stimuli with a frequency of 20-40 cps. The duration of each impulse was 0,1-0,5 milliseconds. The substances were injected intravenously.

The choice of such a method was occasioned by the fact that the more widespread means of testing ganglioplegic agents cannot always be used in a given instance. Thus, to draw conclusions about the ganglion blocking activity of largactil according to the reaction of the effector organ (nictitating membrane, pupil, the action of the heart, etc.) arising in response to irritation of preganglionic fibers is difficult and at times simply impossible (when the substance is injected into the general blood stream). This pertains to both sympathetic and parasympathetic innervation and is caused by the ability of largactil to exert an atropine-like adrenolytic and sympatholytic effect. More expedient for such examinations is the oscillographic method, which permits the derivation of biopotentials directly from the postganglionic fibers or the ganglion while the blood supply of the ganglionic cells is maintained.

RESULTS OF THE EXPERIMENTS

Largactil in a dose of 2,5-5 mg/kg of body weight completely prevented the reaction of the nictitating membrane to irritation of the preganglionic trunk. As is shown in Fig. 1, in this case the biocurrents not only did not decrease, but even increased somewhat in the given experiment. The oscillogram in Fig. 1c, serves as evidence that the substance reaches the cells of the ganglion. The complete absence of biocurrents on it is linked with the use of tetraethylammonium (10 mg/kg), which blocked the transmission of stimulation in the ganglionic synapses. The negligible lowering of biocurrents which was observed in individual cases when large

doses of largactil (of the order of 10-20 mg/kg) were used can be explained by the disturbance to the blood supply of the ganglionic cells in connection with the falling off of blood pressure.

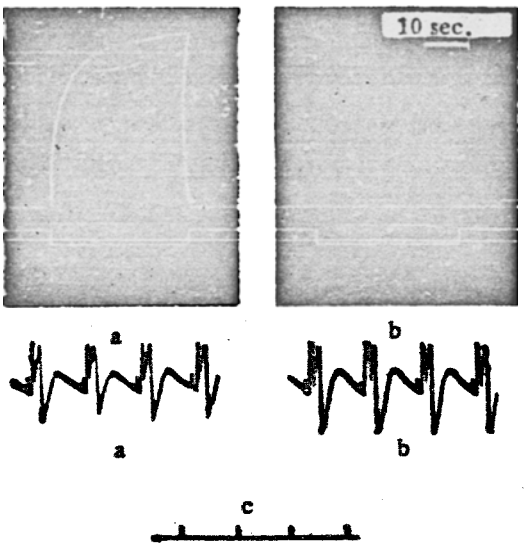

Fig. 1. Simultaneous recording of the contractions of the nictitating membrane and the biocurrents of the postganglionic fibers during electrical irritation of the preganglionic trunk. a) before injection of largactil; b) after injection of largactil, 2.5 mg/kg; c) a minute after injection of tetraethylammonium, 10 mg/kg. Frequency of irritation: 20 cps. Duration of each stimulus: 0.5 milliseconds. Amplitude 1 v. The short vertical lines on the oscillograms are the artifacts of the irritation. The biocurrents corresponding to the mechanograms are designated with the same letters.

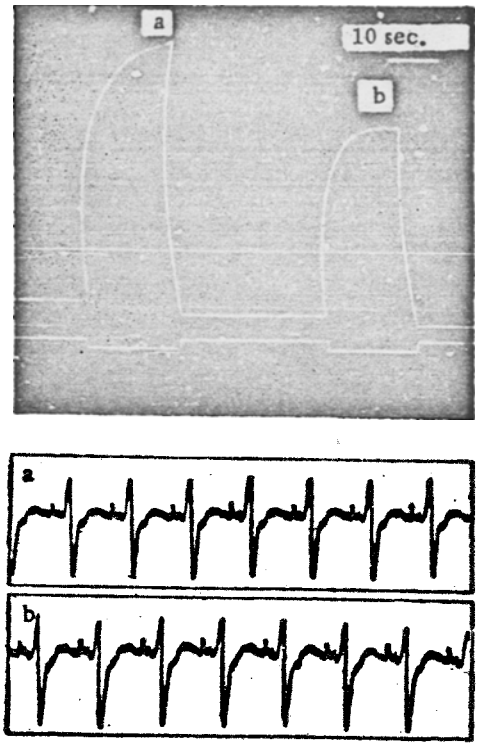

Fig. 2. Simultaneous recording of the contractions of the nictitating membrane and the biocurrents of the postganglionic fibers during electrical irritation of the preganglionic trunk. a) before injection; b) after injection of pacatal, 5 mg/kg. The other designations are the same as in Fig. 1.

Thus the absence of a reaction on the part of the nictitating membrane while the amplitude of the biocurrents remains unchanged attests to the peripheral sympatholytic effect of largactil. Transmission of impulses in the ganglion in this case is not depressed.

Analagous data were obtained also for the other representative of the phenothiazine series, mepazine (pacatal), which was synthesized in the chemistry department of the Institute of Pharmacology and Chemotherapy of the Academy of Medical Sciences of the USSR by S. V. Zhuravlev, A. N. Gritsenko and M. I. Dorokhova. The pharmacology of this agent has been studied by Yu. I. Vikhlyaev [2]. In a dose of 5-10 mg/kg, pacatal as a rule does not exert a depressant influence on the cells of the superior cervical ganglion, a fact which may be inferred from the absence of changes in the biopotentials of the postganglionic fibers (Fig. 2). The reaction of the nictitating membrane following the use of pacatal decreased to a lesser extent than from the use of largactil. This can be perceived in a comparison of Fig. 1 and Fig. 2. Largactil in a dose of 5 mg/kg usually completely prevented contraction of the nictitating membrane, while pacatal in a dose of 5-10 mg/kg decreased it on the average by 10-30%.

Consequently the sympatholytic properties of pacatal are less marked than those of largactil.

The data obtained attest to the fact that largactil and pacatal in so-called therapeutic doses do not exert

a depressant influence on the transmission of stimulation in the superior cervical ganglion. The weakening of the contractions of the nictitating membrane which is observed when these substances are used is the result of their sympatholytic effect. Thus one may conclude that largactil and pacatal do not possess ganglioplegic properties.

SUMMARY

The preganglionic sympathetic trunk of the cat was stimulated by rectangular electric shocks of 20 cps frequency, and the contractions of the nictitating membrane and the biocurrents of the postganglionic fibers of the superior cervical ganglion were simultaneously recorded: neither aminazine (largactil) nor mepazine (pacatal) in doses of 5-10 mg/kg exerts any ganglioplegic effect. Sympatholytic properties of aminazine are more pronounced than those of mepazine.

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* In Russian.