METHODS

A Method for Evaluation of Conduction Anesthesia

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We propose a new method for evaluation of conduction anesthesia in animals: by the degree of prolongation of cardiac cycle during vagus nerve stimulation by solitary electric discharges synchronous to the dominant ECG wave, proximally from the site of anesthetic application on the nerve.

Key Words: *conduction anesthesia; heart; vagus nerve; chronotropic effect*

More than 150 methodological approaches to evaluation of the efficiency of local anesthetics were proposed [1]; on the one hand, this confirms the importance of the task and, on the other, is an evidence of the absence of reliable methods for evaluating surface, infiltration, and conduction anesthesia, each of which should be evaluated objectively. For example, evoked motor or painful reactions serve as the criteria of the studied effect in the majority of conduction anesthesia models [1], but quantitative evaluation of these reactions is difficult, because of their high variability during the experiment. We searched for an optimal method for evaluation of conduction anesthesia.

An assumption that the mechanism of conduction anesthesia does not depend on the type of nerve fibers and hence, its efficiency can be successfully evaluated by suppression of somatic, nociceptive, and autonomic reactions, became the theoretical prerequisite for our study.

The proposed approach is based on evaluation of the chronotropic effect of the vagus nerve (VN) during its stimulation with electric pulses proximally to the site of anesthetic application.

The possibility of drastic prolongation of one cardiac cycle during VN stimulation with electric burst delivered during certain phases of the cardiac cycle, served as the methodological prerequisite of the method. This is a common biological phenomenon and it can be equally effectively reproduced in all laboratory animals.

Special experiments on cats showed that VN stimulation with solitary (no more than 1 burst per 2 min) bursts consisting of 3 supramaximal pulses (2 msec, 40 Hz, 6 thresholds) synchronously with the dominant ECG wave is most convenient from material, technological, and anatomical viewpoints and the optimal as regards the amplitude and reproduction of the chronotropic effect. An important sign of the proposed method is constant body temperature in these animals, because temperature fluctuations notably modify the basal activity of the cardiac cycle used for the evaluation of the chronotropic effect and hence, neurotropic activity of the studied drugs.

In cats subjected to forced ventilation under chloralose-Nembutal narcosis (75+15 mg/kg intraperitoneally) a contact thermometer connected to a 100-W reflector was rectally inserted and body temperature was set up at 37°C. The right (left) VN was then mobilized, ligated, and cut at the level of the thyroid cartilage. The peripheral fragment of the nerve was pinned to bipolar needle electrodes (made from insulin injection needles) with 2.0-2.5 mm distance between the electrodes and embedded in melted mixture of medical wax and vaseline oil. The nerve was put into

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a cuvette (1 cm in diameter and 1 cm deep) with two holes for placing the nerve at a distance of 1.0-1.5 cm from the electrodes. The nerve fragment between the electrodes and the cuvette and the outer side of the cuvette were imbedded in the wax-Vaseline oil mixture, after which the cuvette was filled with Kravkov's solution without glucose (0.9 g NaCl, 0.2 g KCl, 0.2 g $CaCl_2$, 0.15 g $NaHCO_3$, and 100 ml H_2O) and covered with polyethylene film for preventing drying. ECG electrodes (pins) were subcutaneously injected near the heart and into one limb. Recording of intraatrial ECG gives a stronger signal with sharply predominating *P* wave; for this, a fine bipolar tube with 0.5 mm distance between the electrodes was transvenously inserted through the right atrium. The output signal of the electrocardiograph was transmitted to the device which singled out the predominating ECG wave and switched on an electrostimulator generating solitary bursts of electric pulses.

The threshold of the chronotropic effect (usually 0.3-0.4 V), corresponding to 10% prolongation of the cardiac cycle was determined by stimulating the nerve in the periodical mode with electric pulses (2 msec, 40 Hz, 5 sec). This was followed by a single discharge of 3 supramaximum pulses (2 msec, 40 Hz, 6 thresholds) synchronously with the predominating ECG wave and the initial chronotropic effect (ICE, %) was determined by the formula

$$ICE=100\times(T_{n+1}-T_n)/T_n,$$

where T_n is the last cardiac cycle before stimulation and T_{n+1} the first one (msec).

After ICE was evaluated, the saline was sucked from the cuvette and it was filled with similar saline with the anesthetic in the needed concentration. The tested chronotropic effect (TCE, %) was evaluated by the above method every 2 min till the effect attained a plateau. The cuvette was then thoroughly washed and filled with a fresh portion of Kravkov's solution; TCE was evaluated during recovery of nerve conduction. The depth of anesthesia (DA, %) throughout the entire experiment was evaluated by the formula:

$$DA=100\times(ICE-TCE)/TCE.$$

Each concentration of the substance was studied in 5-7 experiments.

Practical use of this method showed its main advantages: the possibility of long-term high-quality recording of the signals reflecting the time course and intensity of conduction anesthesia; the possibility of evaluating conduction anesthesia under conditions of total narcosis, *i.e.* direct chronotropic effect of VN on the heart (not reflex or painful reactions to nerve stimulation) serve as the indicator of local anesthetic activity; clear-cut easily and objectively measured criteria of conduction anesthesia; the possibility of completely automated measurements.

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