INFLUENCE OF VITAMIN K_3 (VICASOL) ON THE ACTION OF CHOLINESTERASE SUBSTANCES*

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According to the literature data [9, 10], vitamin K_3 (methinone; 2-methyl-1,4-naphthoquinone) is a powerful inhibitor of choline acetylase—an enzyme that takes part in the final stage of acetylcholine synthesis. It was shown [11] that vitamin K_3 inhibits the synthesis of acetylcholine of frog brain tissue in concentrations which do not influence the activity of the acetylcholine-cleaving enzyme cholinesterase. It was also established that vitamin K_3 changes the neuromuscular conductivity [5] and prevents the inhibiting action of the vagus nerve on the frog heart [6]. The authors explain all this by a depression of the acetylcholine synthesis.

These data give the basis for the study of the influence of vitamin K_3 preparations on the action of anticholinesterase agents, which are of great significance in pharmacology and toxicology.

The anesthesia-like action of proserine on frogs is explained by its anticholinesterase properties. This leads to the accumulation in the synapses of the central nervous system of concentrations of the acetylcholine liberated there that disrupt the conduction of the nerve impulse in the interneuronal synapses of the central nervous system [1, 7].

In this work we studied the influence of a domestic preparation of vitamin K_3—vicasol (a bisulfite compound of 2-methyl-1,4-naphthoquinone) on the development of an anesthetic-like action of proserine on male lake frogs (R. ridibunda) as well as on the survival rate of adult male white mice (weighing not less than 18 g) after poisoning with proserine, which is a competitive inhibitor of cholinesterase, and with phosphacol, a representative of organophosphorus compounds, which cause irreversible inhibition of cholinesterase activity [8].

TABLE 1. Influence of Preliminary Injection on Viscasol on the Development of Proserine Narcosis in Frogs

Time after injection of proserine (in min)	Number of frogs in which narcosis had time the develop (in %)	
	control	experimental
10	16.7 (10)	16.7 (10)
15	66.6 (40)	33.4 (20)
20	83.3 (50)	33.4 (20)
60	83.3 (50)	33.4 (20)
Narcosis did not set in	16.7 (10)	66.6 (40)

Note. The number of frogs used in the experiment is indicated in parentheses.

PROCEDURE

Viscasol in doses of 37.5 and 75 mg/kg was injected into the submaxillary lymphatic sac of the frogs 20 min before the administration of a proserine solution at the same place. Proserine was administered in a dose of 2.5 mg/kg. Parallel experiments were carried out in which a corresponding volume of distilled water was administered instead of a vicasol solution to frogs of the same catch and of a similar weight and sex, as the control experiments. An indicator of the onset of the narcosis-like state was the inability of the frog, lying on its back, to resume the normal position and the disappearance of the reaction of the jerking-back of the foot stretched out by a forceps.

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TABLE 2. Influences of Vicasol on the Duration of Proserine Narcosis in Frogs

Group of frogs	Number of frogs	Average duration of narcosis (in min) M ± m
Control	10	40 ± 8.02
Experimental	10	10 ± 2.09

TABLE 3. Survival Rate of Proserine-Poisoned White Mice in Treatment with Vicasol

Group	Number of mice		
	total in experiment	died	surviving after 24 h
Control (proserine in a dose of 0.3 mg/kg subcutaneously).	14	14	0
Experimental (proserine + vicasol in a dose of 2 mg/kg subcutaneously).	28	0	28

RESULTS OF THE EXPERIMENTS

The preliminary injection of vicasol substantially reduces the intensity of the development of proserine narcosis. The number of cases in which the action of proserine generally was not manifested was also extremely great (66.6% of the cases in the experimental series as against 16.7% in the control) (Table 1). These differences are statistically quite reliable ($P < 0.001$).

The administration of vicasol to the frogs (30 mg/kg) against a background of the developing action of proserine produces a statistically reliable ($P < 0.01$) decrease in the duration of proserine narcosis (Table 2).

In experiments on white mice, it was established that the administration of the corresponding doses of vicasol against a background of developing symptoms of acute proserine poisoning (tremors) guarantees 100% survival of mice poisoned by the absolute lethal dose of proserine (Table 3).

As for the influence on the outcome of intoxication of mice by phosphacol, we obtained no therapeutic effect from the use of vicasol alone. However, vicasol substantially intensified (potentiated) the therapeutic effect of cholinolytics—atropine and a ganglioblocker, pachycarpine (Table 4). The differences obtained are statistically reliable

TABLE 4. Survival Rate of White Mice Poisoned with Phosphacol in Combined Therapy with Vicasol and Cholinolytics

Preparations used	Number of mice		
	total in experiment	died	surviving after 24 h
Phospacol (3.6 mg/kg intraperitoneally) + atropine (5 mg/kg subcutaneously)	18	12(66.7%)	6(33.3%)
Phosphacol + atropine + vicasol (2 mg/kg subcutaneously)	18	0	18(100%)
Phosphacol + pachycarpine (10 mg/kg subcutaneously)	12	6(50%)	6(50%)
Phosphacol + pachycarpine + vicasol	12	0	12(100%)

($P < 0.01$). The potentiating influence of vicasol is extremely important, since to obtain a therapeutic effect from atropine in poisoning by organophosphorus compounds, it must be administered repeatedly and in amounts substantially exceeding the maximum therapeutic dose [3, 4]. The increase in the therapeutic action of pachycarpine is also of great significance, since, according to the literature data [2], it is rather weak in comparison with the prophylactic effect.

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