

HETEROCID-321 AWAKENING ACTION ON THE MODEL OF KETAMINE ANAESTHESIA

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Introduction. Natural disasters, wars and man-made disasters are accompanied by "traumatic" epidemics. It dramatically increases the role of urgent surgery, which effectiveness depends not only on qualified surgeons, but also the presence of extemporaneous preparations required during operations and rehabilitation activities.

A duration of operation plays an important role in the field conditions. It mainly depends not only on the duration of surgical procedures, but also on a duration of anesthesia that is very individual and varies in the range from 30 minutes to several hours. Due to limited amount of surgical and rehabilitation personnel it is a factor that determines the rate and effectiveness of rescue measures.

Medical preparations which are capable to interrupt anesthesia quickly, efficiently and harmlessly are absent now in the arsenal of modern pharmacology. This makes the development of appropriate drugs particularly an urgent problem.

The aim of our study was to find original substances with the wake-up action in the series of sulfur- and nitrogen-containing heterocycles.

Materials and methods. Evaluation of antinarcosis action (ANA) of the substances under study was performed on nonlinear white mice weighing 20-30g on the model of ketamine anesthesia. Animals were randomized into 4 groups, each received ketamine intra peritoneal (i.p.). The duration of the anesthetic sleep (DAS) of the first group was accepted as a control. At the fifteenth minute of the anesthetic sleep the second group was injected i.p. by Heterocid-321, the third one by the reference drug (sulfokamfokaine), and the fourth one by niketamidum, all of them same i.p. The main indicator of the ANA test substances was the reducing of the DAS (awakening effect).

The reliability of the results was evaluated by the nonparametric Newman-Keuls criteria using the Statistica 10.0 program.

Results and discussion (Table 1). During the studies, it was found that the optimal depth and duration of ketamine anesthesia was achieved at a dose of 150 mg/kg. The substances under study showed a significant awakening effect: Heterocid-321 at a dosage range from 7.5 to 2 mg/kg, sulfokamfokaine - at doses of 70 - 20 mg/kg.

The experiment showed that the DAS has a significant dose-dependence. Heterocid -321 at a dose of 2 mg/kg was 1.4 times more effective than at a dose of 7.5 mg/kg and 1.7 times than at a dose of 3.5 mg/kg. Sulfokamfokaine effectiveness

at 20 mg/kg was higher in 1.5 times and 1.6 times, compared with the drug at doses of 70 and 35 mg/kg, respectively. Niketamidum DAS and other doses of Heterocide - 321 turned out to be statistically insignificant.

Table 1

APA drugs under study on the model of ketamine anesthesia

№	Substances injected to mice	Average DAS		APA,%
1	Ketamine 150 mg/kg (control)	33 minutes 37 seconds 2017,96±110,25 сек	100%	0
2	<i>Heterocide -321 7,5 mg/kg</i>	<i>22 minutes 28 seconds *</i> <i>1288,00±109,47 seconds</i>	<i>62%*</i>	<i>38%</i>
3	<i>Heterocide -321 3,5 mg/kg</i>	<i>26 minutes 33 seconds *</i> <i>1592,50±251,67 seconds</i>	<i>76%*</i>	<i>24%</i>
4	Heterocide -321 2,5 mg/kg	26 minutes 43 seconds 1603,83±168,94 seconds	79%	21%
5	<i>Heterocide -321 2,0 mg/kg</i>	<i>18 minutes 45 seconds *</i> <i>1124,86±153,85 seconds</i>	<i>44,3%*</i>	<i>56,7%</i>
6	Heterocide -321 1,5 mg/kg	32 minutes 54 seconds 1975,33±95,76 seconds	98%	2%
7	Heterocide -321 1,0 mg/kg	29 minutes 36 seconds 1779,33±288,04 seconds	88,2%	12,8%
8	Sulfokamfokaine 70 mg/kg	43 minutes 42 seconds 2899,25±422,30 seconds	130%	+ 30 %
9	Sulfokamfokaine 35 mg/kg	46 minutes 23 seconds 3442,2±197,89 seconds	138%	+ 38%
10	<i>Sulfokamfokaine 20 mg/kg</i>	<i>28 minutes 34 seconds *</i> <i>1767,67±51,74 seconds</i>	<i>85%*</i>	<i>15%</i>
11	Nikethamidum 63 mg/kg	30 minutes 55 seconds 1876,33±21,57 seconds	92%	8 %

Note. * Significant differences from the control index ($p < 0.05$) on parametric Newman-Keuls criterion (Statistica 10.0);

Heterocide-321 substance significantly ($p < 0,05$) shows an expressed awakening effect reducing in 4.4 times the duration of the anesthetic sleep compared to the control group, and at a dose in 10 times lower than that of sulfokamfokaine increases its efficiency by 3.7 times.

Thus, the maximum of Heterocide-321 awakening effect was shown at 2 mg/kg, and for sulfokamfokaine it was 20 mg/kg.

Conclusions. Derivatives of sulfur- and nitrogen-containing heterocycles are prospective for the search of the original substance with wake-up action.