

## MODULATION OF B-LYMPHOCYTES ACTIVITY BY CHOLINOTROPIC DRUGS BEFORE WATER-IMMERSION STRESS

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## МОДУЛЯЦИЯ АКТИВНОСТИ В-ЛИМФОЦИТОВ ХОЛИНОТРОПНЫМИ ПРЕПАРАТАМИ ПЕРЕД ВОДНО-ИММЕРСИОННЫМ СТРЕССОМ

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The aim of the work was to study the effect of modulation of B-lymphocytes activity with cholinotropic drugs on the stomach damage caused by water-immersion stress (WIS). The work was performed on male Wistar rats. Atropine (2 mg/kg), methacin (2 mg/kg) and choline alfoscerat (90 mg/kg) were administered 14 days before the WIS which lasted for 5 hours. The number of antibody-producing cells (APC) in spleen and the content of immunoglobulins IgA, IgG, IgM in blood were determined. The rats injected with saline were served as the control. On day 14 after administration of methacin or choline alfoscerat, but not atropine, an increase in the APC content in the spleen was observed comparing with control. At the same time, there was a significant decrease in the number of gastric ulcers. Thus on the model of water-immersion stress (WIS), it has been shown that B-lymphocytes can serve as a new target for the action of cholinotropic drugs, and modulation of their activity can provide effective prevention against stress.

**Keywords:** water-immersion stress; cholinotropic drugs; B-lymphocytes.

Целью работы явилось изучение влияния модулирования активности В-лимфоцитов холинотропными препаратами на повреждение желудка, вызванного воздействием водно-иммерсионного стресса (ВИС). Работа выполнена на крысах-самцах линии Вистар. Атропин (2 мг/кг), метацин (2 мг/кг) и холина альфосцерат (90 мг/кг) вводили за 14 суток до 5-часового ВИС. В селезенке определяли количество антител-образующих клеток (АОК), в крови — содержание иммуноглобулинов IgA, IgG, IgM. Контролем служили крысы, которым вводили физиологический раствор. На 14 сутки после введения метацина или холина альфосцерата, но не атропина, наблюдалось увеличение содержания АОК в селезенке по сравнению с контролем. При этом происходило существенное снижение числа язв желудка, образующихся в результате ВИС. Таким образом, было показано, что В-лимфоциты являются новой мишенью действия холинотропных препаратов, а модуляция их активности может обеспечивать эффективную профилактику последствий стресса.

**Ключевые слова:** водно-иммерсионный стресс; холинотропные препараты; В-лимфоциты.

**Introduction.** The development of water-immersion stress (WIS) is accompanied by domination of parasympathetic influences, which initiate ischemia and antioxidant stress of stomach [7]. Little attention has been paid to the modulation of the B-lymphocytes activity before the WIS to prevent its negative effects. Earlier we have shown that the use of B-lymphocyte stimulator 14 days before WIS and the stress protective agent 30 minutes before the WIS significantly limit the stomach damage [2]. In addition, it is known that agonists and antagonists of muscarinic and nicotinic acetylcholine receptors (m-, n-AChR) significantly enhance the antibody-producing activity of B-lymphocytes in spleen [3]. It can be assumed that the use of cholinotropic drugs may be an important direction in the development of rational approach to the prevention of the negative effects caused by different prolonged stresses. The aim of the work

was to study the effect of B-lymphocytes modulation by cholinotropic drugs before WIS on the stomach damage.

**Material and methods.** The study was performed on Wistar male rats. The 5-hour WIS was modeled in rats after 24 hours hungry diet [7]. Antagonists of m-AchR atropine (2 mg/kg) and metacin (2 mg/kg), and m- and n-AchR agonist choline alfoscerate (90 mg/kg) were administered 14 days before the WIS. The amount of antibody-producing cells (APC) was determined in the spleen [6]. In peripheral blood the content of immunoglobulins IgA, IgG, IgM were evaluated using commercial enzyme immunoassay kits. The rats treated with saline instead of drugs, were used as control.

**Results and discussion.** The obtained data showed that on the 14th day after the administration of metacin or choline alfoscerate, but not atro-

The effect of cholinotropic agents on antibody production of B-lymphocytes and the number of ulcers in stomach of rats with WIS

Drug	APC/10 <sup>6</sup> splenocytes	IgA (mg/ml)	IgG (mg/ml)	IgM (mg/ml)	Index of gastric damage, points
Control	486 ± 40	0.038 ± 0.004	0.497 ± 0.005	0.046 ± 0.005	3.2 ± 0.2
Atropine, 2 mg/kg	510 ± 45	0.036 ± 0.003	0.503 ± 0.011	0.051 ± 0.008	2.5 ± 0.3
Metacin, 2 mg/kg	2300 ± 34*	0.031 ± 0.002	0.495 ± 0.004	0.054 ± 0.012	1.1 ± 0.2*
Choline alfocerate, 80 mg/kg	1900 ± 42*	0.036 ± 0.002	0.500 ± 0.006	0.049 ± 0.004	1.3 ± 0.1*

Note. \* $p < 0.001$ , 8 rats in group were used for each test.

pine, a high content of APC was determined in the spleen of experimental rats, but the concentrations of IgA, IgG, IgM did not differ from the control. A significant decrease in the number of ulcers in the stomach of these rats was observed (see Table).

We suggest that the most significant adaptive processes occur in the spleen and that the prolonged response of B-lymphocytes may be associated with the action of drug metabolites. It is known that metacin is a benzyl acid-choline ester [1]. Our previous studies of metacin metabolites identifica-

tion showed that its disintegration leads to the formation of pharmacologically inactive 2-hydroxy-2, 2-diphenylacetic acid and pharmacologically active choline [5]. The drug choline alfocerate splits into glycerophosphate and choline. Choline is an agonist of all AChR cell subtypes [1], and apparently can provide a prolonged effect of the drugs.

**Conclusion.** Thus B-lymphocytes can serve as a new target for the action of cholinotropic drugs, and modulation of their activity can provide effective prevention against stress.

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