Influence of environmental factors on the contractile activity of the lymphatic system

Biology and Medicine

Research Article
Introduction

It is important to conduct toxicity studies in the lymphatic system, since it is a part of the cardiovascular system. However, nowadays, this system of the body is poorly understood.

The study of physiology problems and pathology of adaptation mechanisms in the cardiovascular system has a paramount importance, as the cardiovascular system is included in the reaction of adaptation in pathological conditions and plays a significant role to maintain homeostasis in the new environmental conditions.

Numerous studies have showed the role of the various divisions of the spinal cord and brain in the regulation and formation of lymph [2-4].

It is known that vasomotor innervation has no direct contact to the end sections of nerve fibers with smooth muscle cells. Neurotransmitters are formed at the ends of the autonomic nerve fibers and then they are innervated. Then, they act on the smooth muscle cells longer in comparison with the action in somatic nerve endings. Influence of neural transfer on effector cells is done by diffusion of the mediator in the smooth muscle cells of visceral organs. They have postsynaptic membranes comparing with somatic muscles, so the effects of visceral nervous control systems on the structure are similar to the effects of humoral mechanisms [5,6].

Currently, Baikonur cosmodrome in Kazakhstan is one of the active spaceports in the world and negative effects of hydrazine derivatives have caused a big issue in the country. A functional change of the internal organs of the effect of environmental factors reveals mechanisms of action, and thus helps to understand the pathogenesis of intoxication under the influence of various xenobiotics. Therefore, we aimed...
to study the contractile activity of the lymphatic system during hydrazine derivatives intoxication.

Hydrazine derivatives are dangerous for any types of exposure, because they have long-term and specific effects and particularly they cause tumors in organs and tissues of animals [7]. Toxicity of selected compounds in this series is different to a considerable extent; it depends on the type of animal. Also, according to the authors, toxicity is independent on the way of administration among the species, which reflects the rapid absorption of hydrazine and its derivatives of the sites of application [8]. The evidence of the high toxicity hydrazine derivatives is determined by concentration value with reference to 1.1 DMG and MMG in animal experiments. Since the threshold of acute effect of DMG 1.1 Mouse – 15 mg/m$^3$, the threshold of chronic inhalation action 1.1 DMG 0.17 mg/m$^3$; MMG – 0.015 mg/m$^3$ [9].

The study about the impacts of hydrazine on living organisms has become important in the country with the space activities development in engineering and technology [10-12]. The study of many researchers showed that phenylhydrazine affects the cholesterol metabolism in the blood serum during seed phenylhydrazine is accompanied by bone marrow hyperplasia after hemolysis [13]. Also, other studies described a direct impact on NDMA cellular proteins that involved in apoptosis cells and it explained the genetic activity of these substances [14,15].

It is quite interesting that in the past Canada researchers practiced unconventional cancer treatments with hydrazine sulfates. Although the previous study had proved that eleven hydrazine derivatives, aromatic amines showed direct mutagenicity and toxicity toward Salmonella Typhimurium and associated mutagenic process such derivatives as – phenylhydrazine, 2-nitro-phenyl-hydrazine, 4-nitrophenylhydrazine, 2,4-dinitrophenylhydrazine, p-toli hydrazine, and 4-nitroaniline [16].

The studies also showed that treatment by NDMA caused acute toxicity [17]. As a result, it led to the destruction of cell membranes and changes in protein profile in rats [12].

Materials and Methods

Albino rats were used as the objects of the experiment. The weight of these rats was 250-300 g. Experimental animals were divided into five groups. Table 1 illustrates the outline of separation of groups, substances that were used to them. The chosen rates were male and drugs were introduced intragastrically (by gavage).

The contractile activity of lymphatic vessels and lymph nodes was studied by the standard technique.

Animals were anesthetized. Then, there was isolation of the thoracic duct (Ductus thoracicus). Afterward, they were purified from extraneous tissues. Preparations were fixed by loops of a thin thread on the vertical axis of the vessel and the nodes that had been used to attach the preparations to the camera's hook and mechatronick's rod. Preparations were put in the camera with well-drained oxygenated Krebs' solution that had been incubated in a constant temperature of 37ºC in ultrathermostat UT-01. Volume of camera was 2 × 3 cm. Preparations were studied by the common method in installation. Isometric tension of preparations was checked on the tape recorder with the help of mechatronon MCH-1C. There was scientific research about characteristics of the spontaneous rhythmic activity of the thoracic duct and visceral lymph nodes. Moreover, there was the assessment of the frequency and amplitude of spontaneous rhythmic contractions. The one side of the end of longitudinal cuts of lymphatics was fixed to the bottom of the vertical type of thermostatic camera, and another one was set to the force sensor (mechantronon 6Mch × 1B, 6Mch × 2B). There was purification of fat and extraneous tissue. After that, 10 mm of isolated segments of ileum and lymph nodes were fixed

<table>
<thead>
<tr>
<th>Group 1 (control)</th>
<th>Volume</th>
<th>Substance</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 2 (acute)</td>
<td>1 ml</td>
<td>H$_2$O</td>
<td>–</td>
</tr>
<tr>
<td>Group 3 (acute)</td>
<td>18.8 mg/kg</td>
<td>Phenylhydrazine</td>
<td>Once</td>
</tr>
<tr>
<td>Group 4 (chronic)</td>
<td>18.8 mg/kg</td>
<td>Phenylhydrazine</td>
<td>3 months</td>
</tr>
<tr>
<td>Group 5 (chronic)</td>
<td>18.8 mg/kg</td>
<td>Phenylhydrazine</td>
<td>3 months</td>
</tr>
</tbody>
</table>

Table 1: The scheme of distribution of substances in different group animals.
by loops from thin filaments that had been used for setting preparations to the static camera’s hook and mechanotronic’s rod.

Krebs solution was used to the isolated smooth muscle preparations in rats: NaCl – 133.0; NaHCO$_3$ – 16.3; NaH$_2$PO$_4$ – 1.38; KCl – 5; CaCl$_2$ – 2.5; MgCl$_2$ – 0.1; glucose – 7.8 mM/L; pH – 7.4 (the temperature was +37°C).

Nutrient solutions were oxygenated with the gas mixture: 95% O$_2$ and 5% CO$_2$.

The following pharmacological agents were used: adrenaline–hydrochloride ($5 \times 10^{-9} – 1 \times 10^{-5}$ M). The following pharmacological blockers were used to study the nature of vascular receptors: pyrroxanum ($1 \times 10^{-5}$ M) – antagonist of α-adrenergic receptors; obzidian ($1 \times 10^{-5}$ M) – antagonist of β-adrenergic receptors. Program SI on a personal computer recorded spontaneous or induced contractile activity of isolated vascular preparations. Statistical data were analyzed by Student’s t-test.

Results and Discussion

The regime of sustaining vital functions of isolated preparations, the intervals of introducing agents and the order of laundering substances was kept in each experiment.

Currently, there are lots of articles about the impact of hydrazine and its derivatives on the lymphatic system in medical and biological literature. It shows that the lymphatic system plays an important role in the system of the body. It can drainage bodies and has natural filter function. It is believed that lymphatic system is the immunological basis of the organism.

The changes of features contractile rhythmic activity of lymphatic vessels depend on the condition of the organism, slagging of the bodies, and the presence of various alien objects in the body.

The aim of the study was to identify the changes of the frequency amplitude of spontaneous rhythmic contractions of the thoracic duct at acute and chronic intoxication with phenylhydrazine and on the correction drug Salsocollin.

The experiment on isolated preparations showed a series of spontaneous rhythmic contractions. The frequency of spontaneous rhythmic contractions of the thoracic duct on control animals was $6.2 \pm 0.01$ cuts/min and the amplitude of spontaneous rhythmic contractions was $6 \pm 0.4$ mg.

Acute intoxication with phenylhydrazine on animals showed a significant inhibition of spontaneous rhythmic contractions of the thoracic duct: the frequency was reduced by 62.74%, while the amplitude is decreased by

**Figure 1:** Frequency-amplitude feature of spontaneous rhythmic contractions of the thoracic duct in acute and chronic intoxication with the hydrazine derivatives.
25.66% ($p < 0.01$). In comparison with controls, the animals with Salsocollin drug decelerated the rate to 40.5% ($p < 0.001$) and suppressed the amplitude to 12.4% ($p < 0.05$) (Figure 1).

Chronic intoxication of animals with phenylhydrazine showed the suppression of spontaneous rhythmic contractions of thoracic duct as following: frequency was reduced by 45.5% ($p < 0.001$) and the amplitude was decreased by 36.1% ($p < 0.01$). In comparison with controls, the animals with Salsocollin decelerated the rate to 18.3% ($p < 0.001$) and suppressed the amplitude to 22.8% ($p < 0.05$) (Figure 1). It can be seen that current substance is quite aggressive to the thoracic duct, as a result it can lead to the depression or stop of the movement of lymph in the vessel (Figure 1).

The result of experiment showed that phenylhydrazine inhibited contractile activity of lymphatic duct, while Salsocollin reduced the negative effect of hydrazine derivatives on the contractile activity of the thoracic duct.

The next step was to study the responses of isolated smooth muscle preparations of thoracic duct to the adrenaline on intoxication with phenylhydrazine and on the correction with Salsocollin. $1 \times 10^{-9} - 1 \times 10^{-5}$ M/l of concentration of adrenaline caused a dose-dependent increase

![Figure 2: The response of thoracic duct of rats in the control group at different concentrations of adrenaline.](image)

a – $5 \times 10^{-5}$; b – $1 \times 10^{-5}$; c – $1 \times 10^{-4}$; d – $1 \times 10^{-3}$; e – $1 \times 10^{-2}$; f – $1 \times 10^{-1}$; g – $1 \times 10^{0}$; h – $1 \times 10^{1}$ M/l. Arrow (↓) shows the moment of introduction.
in the frequency of rhythmic contractions. It also led to growth of amplitude to the small concentration of adrenaline and decrease in the large concentration of adrenaline in isolated preparations of the control animals (Figure 2).

$5 \times 10^{-9}$ M of concentration of adrenaline accelerated the rhythmic contractions to $9.6\% \pm 0.1$ and decreased the amplitude to $16.45\% \pm 1.2$; $1 \times 10^{-5}$ M of concentration of adrenaline accelerated the rhythmic contractions to $61.27\% \pm 6.4$ and decreased the amplitude to $31.36\% \pm 2.1$ (Figure 2).

Figure 3 illustrates the acute toxicity of phenylhydrazine in group 2 animals. It can be noted that in this toxicity of phenylhydrazine in response to adrenaline the frequency of rhythmic contractions increased to a lesser degree and amplitude is below the level of response control preparations by 68% (Figure 3a and 3b).

Preparations of group 3 showed an increase of the frequency control range and increased at a rate higher than the amplitude of the data group 3 by 45% (Figure 3a and 3b).

There was a higher growth of frequency of rhythmic contractions in response to adrenaline in group of animals with chronic toxicity with phenylhydrazine than in control animals. The amplitude of rhythmic contractions in this group of experimental animals was suppressed in response to adrenaline by 62% (Figure 3a and 3d).

Group 5 showed a higher growth of frequency of rhythmic contractions in response to adrenaline in comparison with control animals.

Figure 3: The effect $1 \times 10^{-6}$ M/l of concentration of adrenaline on contractile activity of thoracic duct in different group of animals.

(a) Control group of animals; (b) group obtaining phenylhydrazine in the acute experiment; (c) group receiving phenylhydrazine on background corrector in the acute experiment; (d) group receiving phenylhydrazine in chronic experiment; (e) group that received phenylhydrazine on background corrector in chronic experiment.
The amplitude of the rhythmic contractions of the flow in this group of animals was higher to 35% than poisoning animals (Figure 3a and 3e).

There was tonic contraction under the action of adrenaline ($1 \times 10^{-6}$ M/l) with $\beta$-obsidanadrenoblocker ($1 \times 10^{-5}$ M/l). At the same time, there was an inhibition of rate of spontaneous phase contraction of the thoracic duct in control animals to 27.5% ($p < 0.05$), while the amplitude was increased to 56.89% ($p < 0.01$) in the thoracic duct of intact rats.

Group 2 (acute toxicity) and group 4 (chronic toxicity) showed the acceleration of...
reduction of 55.8% (p < 0.01) and 20.8%, respectively. The amplitude decreased to 42.5% (p < 0.001) and 36.9% (p < 0.001) in group 2 and group 4, respectively.

Adrenaline with obsidian caused acceleration of 35.4% (p < 0.001) and increased the amplitude of rhythmic contractions of segments of the lymphatic duct to 25.8% in group 2. Due to introduction of Salsocollin drug in chronic toxicity, adrenaline with obsidian increased the frequency of rhythmic contractions of the lymphatic flow by 15.7% and led to the growth of the amplitude by 22.3% (Figures 4 and 5).

1 \times 10^{-6} \text{M/l} concentration of adrenaline with \(\alpha\)-adrenoreceptor blockade of pyrroxanum (1 \times 10^{-5} \text{M/l}) in intact animals and in animals intoxicated with phenylhydrazine led to a reduction in the tone of smooth muscle preparations.

Adrenaline with pyrroxanum (1 \times 10^{-5} \text{M/l}) accelerated the rhythmic contractions of the lymphatic duct to 87.27% (p < 0.01) and suppressed the amplitude of contractions to 22.41% (p < 0.05) in control animals.

Group 2 showed suppression of the frequency to 15.8% (p < 0.05) and suppression of the amplitude to 15.21% of rhythmic contractions of the duct in response to adrenaline with \(\alpha\)-adrenoreceptor blockade of pyrroxanum in acute intoxication (Figure 5).

There was suppression of amplitude to 70.21% (p < 0.01) and inhibition of frequency to 57.9% (p < 0.001) of rhythmic contractions of the duct in response to adrenaline with pyrroxanum in chronic intoxication by phenylhydrazine. Group 3 indicated the suppression of the amplitude to 36.2% (p < 0.01) and acceleration of rhythmic activity to 45.82% acute intoxication.

At the same time, chronic intoxication in group 3 showed the increase of frequency to 56.7% (p < 0.05) and suppression of the amplitude to 23.84% (p < 0.05) of rhythmic contractions of the thoracic duct.

Conclusion

Thus, it can be seen that adrenaline and its antagonists can suppress the contractile activity of thoracic duct at intoxication with phenylhydrazine. Moreover, suppression of this function of thoracic duct leads to disorder of receptor system of myocyte membrane.

According to experimental data, it can be noted that usage of blockers caused the inhibition of alpha-adrenergic receptors by hydrazine in chronic intoxications. Also, it can suppress function of alpha and beta-blockers in acute toxicity [18].

According to the empirical results, it can be concluded that the treatment of animals with phenylhydrazine leads to suppression of the contractile activity of the thoracic duct in acute and chronic toxicity. The experiment data shows that these changes are associated with the disorder of receptor level of neurohumoral regulation of the vessel.

Under the action of hydrazine, the transport function of thoracic duct was suppressed to 40%, therefore, there was a decrease in the return of proteins from tissues to lymph [19].

References


