Introduction

Water is necessary for the development of life and survival [1, 8, 10, 13, 24], this is its participation in metabolism, facilitation of cellular metabolism [3, 22], modulation of normal osmotic pressure, maintenance of electrolyte balance, regulation of body temperature and many others physiological processes [9, 19, 23]. It has been proven that both excessive and insufficient water consumption has a negative effect on the health of our body [2, 11, 14, 26, 28]. Dehydration reduces a person's ability to engage in physical activity and increases the risk of diseases of the cardiovascular, genitourinary and digestive systems. The endocrine system is involved in a number of water metabolism processes, optimizing the flow and excretion of fluid in the body. The pancreas, as an
organ of the digestive and endocrine systems, undergoes pronounced structural changes under conditions of dehydration [4, 5, 7], as well as during the use of alcohol, opioids and smoking [15, 18, 20, 21, 27]. Therefore, an important issue today is the understanding of risk factors, physiological and pathogenetic links of pancreas diseases, systematization and expansion of data in the world literature on this issue [6, 16, 20, 25].

The aim of the study was to study in the experiment the morphometric features of structural transformations of changes in the parenchyma of the pancreas under the influence of sublethal degree of general, cellular and extracellular dehydration of the organism with the subsequent period of readaptation and correction.

Materials and methods

To achieve the goal of the experiment, 70 laboratory male adult rats weighing from 160 to 200 g were used, which were in the vivarium of the Medical Institute of Sumy State University. The experiment was conducted in compliance with the main provisions of the Council of Europe Convention on the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (March 18, 1986), EEC Directive 9609 (November 24, 1986), Resolution of the First National Congress on Bioethics "General ethical principles of animal experiments" (2001), and orders of the Ministry of Health of Ukraine №690 from 23.09.2009, №944 from 14.12.2009, №616 from 03.08.2012 and the laws of Ukraine.

60 rats were divided into 3 experimental groups, each of which included 20 rats with a simulated sublethal degree of different types of dehydration according to the methods of A.D.Soboleva, V.Z.Sikora, J.Ya.Bodnar, proposed in 1975. Subsequently, the animals of each group were divided into subgroups of 10 rats, which were transferred to the usual drinking diet for 14 days, and those that in addition to the usual drinking diet for the same period received thiazotic acid morpholinium salt in a dose of 0.1 ml as a preparation corrector of morphological changes that occurred during the experiment. The calculation of the dose of the preparation for animals was performed taking into account the recommendations of Y.R. Rybolovlev and R.S. Rybolovlev [17]. The control group included 10 rats.

Pancreas material collection, fixation, and sample fabrication were performed according to traditional methods [11]. To determine the structural components of the gland, paraffin sections 5-7 µm thick were stained with hematoxylin-eosin and Van Gieson. Micropreparations were investigated using a digital image output system "SEO Scan Lab 2.0" (Ukraine).

Morphometric analysis included Langerhans islet area (AIL), pancreatic acinus area (PA), pancreatocyte area (PAC), pancreatocyte nuclei area (PCN), pancreatocyte cytoplasm area (PCAC), and nuclear-cytoplasmic ratio (NCR) determination.

The results of morphometric measurements were processed using the statistical program IBM SPSS Statistic 21. In order to verify the normality of the distribution used Kolmogorov-Smirnov test, the average values are presented as M±m. The Mann-Whitney test was used to compare the performance in the experimental groups. Statistically significant indicators were considered under the condition p<0.05.

Results

In rats of the control group, the average size of AIL (area of islets of Langerhans) was 13934.1±636.92 µm², PA (pancreatic acinus area) - 983.4±67.1 µm²; PAC (pancreatocyte area) - 149.5±3.16 µm²; PCN (pancreatocyte nuclei area) - 10.70±0.41 µm²; PCAC (pancreatocyte cytoplasm area) - 138.7±4.72 µm²; NCR (nuclear-cytoplasmic ratio) - 8.200±0.980 (Fig. 1).

Under the influence of sublethal degree of different types of dehydration, pronounced structural changes were observed in all experimental groups (Fig. 2).

Under the influence of sublethal degree of general dehydration and the period of further readaptation, there was a decrease in the area of AIL - by 3.5% (p=0.880), PA - by 1.4% (p=1.0), PAC - by 1.96% (p=0.571), PCAC - by 1.42% (p=0.650), PCN - by 6.7% (p=0.151), NCR - by 5.93% (p=0.364). Under the conditions of using the thiazotic acid morpholinium salt, we observed a decrease in AIL - by 32.27% (p<0.001), PA - by 15.91% (p=0.041), PAC - by 7.42% (p=0.096), PCAC - by 6.21% (p=0.290), PCN - by 17.82% (p=0.038), NCR - by 12.71% (p=0.406). Comparing the periods of readaptation and correction, a decrease in Langerhans islet area by 29.8% (p<0.001), acinus area - by 14.67% (p=0.019), pancreatocyte area - by 5.57% (p=0.051), pancreatocyte cytoplasm area - by 4.85% (p=0.406), pancreatocyte nuclei area - by 11.97% (p=0.290), nuclear-cytoplasmic ratio - by 7.2% (p=0.597). Detailed morphometric changes in the parenchyma of the pancreas under the sublethal degree of general dehydration, the period of subsequent readaptation and correction are shown in Table 1.

Under the influence of sublethal degree of cellular dehydration, a decrease in the acini area by 23.09% (p<0.001), acinus area - by 12.7% (p=0.019), pancreatocyte area - by 5.57% (p=0.051), pancreatocyte cytoplasm area - by 4.85% (p=0.406), pancreatocyte nuclei area - by 11.97% (p=0.290), nuclear-cytoplasmic ratio - by 7.2% (p=0.597). Detailed morphometric changes in the parenchyma of the pancreas under the sublethal degree of general dehydration, the period of subsequent readaptation and correction are shown in Table 1.

![Fig. 1. Pancreas of the rat from control group: 1 - islet of Langerhans, 2 - acini. Hematoxylin-eosin. x400.](image-url)
dehydration and the period of readaptation, there was a decrease in AIL - by 2.86% ($p_{1}=0.880; p_{2}<0.001; p_{3}<0.001$), pancreatocyte nuclei area - by 10.55% ($p_{1}=1.0; p_{2}=0.041; p_{3}=0.019$), nuclear-cytoplasmic ratio - by 16.22% ($p_{1}=0.112; p_{2}=0.199; p_{3}=0.112$), and increase of acinus area by 2.49% ($p_{1}=0.705; p_{2}=0.762$), pancreatocyte area - by 2.82% ($p_{1}=0.364; p_{2}=0.364$), pancreatocyte cytoplasm area - by 6.47% ($p_{1}=0.041; p_{2}=0.041$).

Under the conditions of simultaneous use of the thiazotic acid morpholinium salt, we observed a decrease in AIL - by 24.85% ($p_{1}<0.001; p_{2}<0.001; p_{3}<0.001$), PCN - by 25.62% ($p_{1}=0.001; p_{2}=0.041$), NCR - by 42.26% ($p_{1}=0.001; p_{2}=0.041$), and increase of PA - by 6.69% ($p_{1}=0.001; p_{2}=0.041$), PAC - by 17.45%, PСAC - by 28.79% ($p_{1}<0.001; p_{2}<0.001$). Comparing the periods of readaptation and correction revealed a decrease in AIL (Langerhans islet area) - by 22.63% ($p_{1}=0.013; p_{2}=0.041$), PCN (pancreatocyte nuclei area) - by 16.85% ($p_{1}=0.130; p_{2}=0.041$), NCR (nuclear-cytoplasmic ratio) - by 31.08% ($p_{1}=0.001; p_{2}=0.041$), and increase of PA (acinus area) - by 4.35% ($p_{1}=0.406; p_{2}=0.406$), PAC (pancreatocyte area) - by 14.22% ($p_{1}=0.001; p_{2}=0.001$), PСAC (pancreatocyte cytoplasm area) - by 20.96% ($p_{1}=0.001; p_{2}=0.001$). Detailed morphometric changes in the parenchyma of the pancreas conditions of sublethal degree of cellular dehydration, the period of subsequent readaptation and correction are shown in Table 2.

Under the influence of sublethal degree of extracellular dehydration and the period of subsequent readaptation, there was an increase in AIL - by 7.04% ($p_{1}=0.130; p_{2}=0.041$), PA - by 3.16% ($p_{1}=0.001; p_{2}=0.041$), PAC - by 10.9% ($p_{1}=0.001; p_{2}=0.041$), PСAC - by 19.57% ($p_{1}=0.001; p_{2}=0.041$), and reducing of PCN - by 16.42% ($p_{1}=0.001; p_{2}=0.041$), NCR - by 31.61% ($p_{1}=0.001; p_{2}=0.041$). Under the conditions of simultaneous use of the thiazotic acid morpholinium salt, we observed an increase in AIL - by 17.04% ($p_{1}=0.001; p_{2}=0.041$), PA - by 9.84% ($p_{1}=0.001; p_{2}=0.041$), PAC - by 18.93% ($p_{1}=0.001; p_{2}=0.041$), PСAC - by 34.71% ($p_{1}<0.001; p_{2}<0.001$), and reducing of PCN - by 16.76% ($p_{1}=0.001; p_{2}=0.001$) and only nuclear-cytoplasmic ratio and reduced by 25.77%.

**Table 1.** Morphometric changes of islets, acini and pancreatocytes under conditions of sublethal degree of general dehydration, period of readaptation and correction.

| Indicator | Control | Severe dehydration | Readaptation | Correction |
|-----------|---------|-------------------|--------------|------------|
| AIL, µm²  | 13934.1±636.92 | 31280.9±1992.7 | 30176.7±1144.1 | 21184.01±1992.1 |
| $p_{1}=0.880; p_{2}<0.001; p_{3}<0.001$ |
| PA, µm²  | 983.4±67.1 | 1326.2±69.7 | 1307.4±64.1 | 1115.5±34.9 |
| $p_{1}=1.0; p_{2}=0.041; p_{3}=0.019$ |
| PAC, µm² | 149.5±3.16 | 172.4±5.8 | 169.0±5.0 | 159.6±5.1 |
| $p_{1}=0.571; p_{2}=0.096; p_{3}=0.151$ |
| PCAC, µm² | 138.7±4.7 | 154.5±5.9 | 152.3±5.2 | 144.9±5.4 |
| $p_{1}=0.650; p_{2}=0.290; p_{3}=0.406$ |
| PCN, µm² | 10.76±0.41 | 17.91±0.52 | 16.69±1.14 | 14.65±0.94 |
| $p_{1}=0.151; p_{2}=0.038; p_{3}=0.290$ |
| NCR, % | 8.270±0.984 | 11.80±0.83 | 11.11±0.92 | 10.31±0.93 |
| $p_{1}=0.364; p_{2}=0.406; p_{3}=0.597$ |

**Notes:** $p_{1}$ - the probability of differences in the indicators of severe general dehydration and the period of readaptation; $p_{2}$ - probability of differences in indicators of severe general dehydration and correction period; $p_{3}$ - the probability of differences in readaptation and correction. AIL - Langerhans islet area; PA - pancreatic acinus area; PAC - pancreatocyte area; PСAC - pancreatocyte cytoplasm area; PCN - pancreatocyte nuclei area; NCR - nuclear-cytoplasmic ratio.

**Fig. 2.** The islet of Langerhans of the rat pancreas: 1 - under conditions of general dehydration, 2 - cellular dehydration, 3 - extracellular dehydration. Hematoxylin-eosin. х200.
Detailed morphometric changes in the parenchyma of the pancreas conditions of sublethal degree of extracellular dehydration, the period of subsequent readaptation and correction are shown in Table 3.

**Table 2.** Morphometric changes of islets, acini and pancreatocytes under conditions of sublethal degree of cellular dehydration, period of readaptation and correction.

| Indicator                  | Control                   | Severe dehydration | Readaptation   | Correction     |
|----------------------------|---------------------------|--------------------|----------------|---------------|
| AIL, µm²                   | 13934.1±636.9             | 25774.2±1316.3     | 25035.6±979.6  | 19368.6±701.3 |
| p<0.076; p<0.001; p<0.001 |                           |                    |                |               |
| PA, µm²                    | 983.4±67.1                | 800.8±57.2         | 820.8±33.1     | 856.6±29.1    |
| p<0.076; p<0.001; p<0.001 |                           |                    |                |               |
| PAC, µm²                   | 149.5±3.1                 | 95.7±1.25          | 98.4±1.79      | 112.4±2.8     |
| p<0.019; p<0.001; p<0.001 |                           |                    |                |               |
| PCAC, µm²                  | 138.7±4.7                 | 75.75±1.29         | 80.61±1.59     | 97.52±2.53    |
| PCN, µm²                   | 10.76±4.1                 | 19.94±1.23         | 17.81±1.31     | 14.81±1.18    |
| NCR, %                     | 8.24±1.09                 | 26.54±1.93         | 22.22±1.79     | 15.29±1.22    |
| p<0.011; p<0.001; p<0.001 |                           |                    |                |               |

**Notes:** p< - the probability of differences in the indicators of severe cellular dehydration and the period of readaptation; p< - the probability of differences in the indicators of severe cellular dehydration and the correction period; p< - the probability of differences in readaptation and correction. AIL - Langerhans islet area; PA - pancreatic acinus area; PAC - pancreatocyte area; PCAC - pancreatocyte cytoplasm area; PCN - pancreatocyte nuclei area; NCR - nuclear-cytoplasmic ratio.

**Table 3.** Morphometric changes of islets, acini and pancreatocytes under conditions of sublethal degree of extracellular dehydration, period of readaptation and correction.

| Indicator                  | Control                   | Severe dehydration | Readaptation   | Correction     |
|----------------------------|---------------------------|--------------------|----------------|---------------|
| AIL, µm²                   | 13934.1±636.9             | 10925.41±655.25    | 11695.4±385.01 | 12787.4±246.1 |
| p<0.131; p<0.013; p<0.059 |                           |                    |                |               |
| PA, µm²                    | 983.4±67.1                | 784.3±29.2         | 809.1±31.1     | 861.5±27.00   |
| p<0.046; p<0.082; p<0.226 |                           |                    |                |               |
| PAC, µm²                   | 149.5±3.16                | 86.14±3.59         | 95.49±2.51     | 102.4±2.9     |
| p<0.070; p<0.007; p<0.096 |                           |                    |                |               |
| PCAC, µm²                  | 138.7±4.7                 | 65.41±3.76         | 78.21±2.82     | 88.12±3.31    |
| p<0.023; p<0.001; p<0.038 |                           |                    |                |               |
| PCN, µm²                   | 10.74±0.41                | 20.74±0.85         | 17.30±0.62     | 14.40±0.65    |
| p<0.005; p<0.001; p<0.010 |                           |                    |                |               |
| NCR, %                     | 8.27±0.98                 | 32.87±2.61         | 22.51±1.34     | 16.69±1.22    |
| p<0.003; p<0.001; p<0.005 |                           |                    |                |               |

**Notes:** p< - the probability of differences in the indicators of severe extracellular dehydration and the period of readaptation; p< - the probability of differences in the indicators of severe extracellular dehydration and the correction period; p< - the probability of differences in readaptation and correction. AIL - Langerhans islet area; PA - pancreatic acinus area; PAC - pancreatocyte area; PCAC - pancreatocyte cytoplasm area; PCN - pancreatocyte nuclei area; NCR - nuclear-cytoplasmic ratio.

Water is one of the main components of the human body, which is vital for the performance of physiological processes, thermoregulation, and transport of nutrients [1, 6, 7, 8]. Water consumption is influenced by numerous factors, including temperature, humidity, as well as the level of physical activity and lifestyle [15, 18, 21, 27]. The most vulnerable groups to dehydration are children and adolescents, who are prone to excessive water loss, especially during physical activity and may not be aware of the need to restore lost fluid [26, 28].

Numerous literature data confirm that disability and mortality from cardiovascular diseases and diseases of the gastrointestinal tract are inversely proportional to water intake [10, 14, 19, 25].

Analyzing the results, it was found that the histostructure of the pancreas, endocrine system and gastrointestinal

(p=0.005). Detailed morphometric changes in the parenchyma of the pancreas conditions of sublethal degree of extracellular dehydration, the period of subsequent readaptation and correction are shown in Table 3.

**Discussion**

Water is one of the main components of the human body, which is vital for the performance of physiological processes, thermoregulation, and transport of nutrients [1, 6, 7, 8]. Water consumption is influenced by numerous factors, including temperature, humidity, as well as the level of physical activity and lifestyle [15, 18, 21, 27]. The most vulnerable groups to dehydration are children and adolescents, who are prone to excessive water loss, especially during physical activity and may not be aware of the need to restore lost fluid [26, 28].

Numerous literature data confirm that disability and mortality from cardiovascular diseases and diseases of the gastrointestinal tract are inversely proportional to water intake [10, 14, 19, 25].

Analyzing the results, it was found that the histostructure of the pancreas, endocrine system and gastrointestinal

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tract, undergoes pronounced structural changes under the influence of sublethal degree of various types of dehydration, which coincides with the data of L.M. Davydova with co-authors (2017), who noted similar morphological changes in the structural components of the tongue in violation of water-electrolyte balance [4]. The absence of significant differences in indicators in the experimental groups under the influence of sublethal dehydration and the period of readaptation was established.

However, under conditions of sublethal degree of general dehydration and the subsequent period of correction with the thiazotic acid morpholinium salt, statistically significant changes were detected in the form of a decrease in the areas of the islets of Langerhans, acini and exocrinocyte nuclei. Comparative analysis of the size of the results of the periods of readaptation and correction showed significant changes in the area of the islets of Langerhans and the area of the acini.

Analysis of the sublethal degree of cellular dehydration and the subsequent period of correction with the thiazotic acid morpholinium salt revealed a significant increase in the areas of exocrinocytes and cytoplasm of exocrinocytes, with a simultaneous decrease in the areas of islets of Langerhans, nuclei of exocrinocytes and nuclear cytoplasm. The obtained results of the periods of readaptation and correction show statistically significant changes in the indicators of the areas of the islets of Langerhans, exocrinocytes, cytoplasm of exocrinocytes and nuclear-cytoplasmic ratio.

However, under conditions of sublethal degree of extracellular dehydration and the subsequent period of correction, significant changes in the areas of islets of Langerhans, exocrinocytes and cytoplasm of exocrinocytes in the form of their increase, with a probable decrease in the area of exocrinocyte nuclei and nuclear cytoplasmic ratio. Comparison of readaptation and correction indicators shows statistically significant changes in the indicators of cytoplasm areas of exocrinocytes, exocrinocyte nuclei and nuclear-cytoplasmic ratio.

Prospects for further research are to study the ultramorphometric characteristics of the parenchyma of the pancreas under different types of dehydration.

Conclusions
1. The use of thiazotic acid morpholinium salt as a corrective drug for changes that have occurred under conditions of various types of dehydration of the body, leads to a reliable leveling of changes in the structural components of the pancreatic parenchyma, compared with readaptation.
2. The most reversible changes that are easier to correct are observed in conditions of general dehydration, while the deepest changes that are most difficult to correct are found in conditions of extracellular dehydration.

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ПОДАЛЬШОЇ РЕАДАПТАЦІЇ ТА КОРЕКЦІЇ
КІЛЬКІСНІ ЗМІНИ МІКРОСТРУКТУРИ ПІДШЛУНКОВОЇ ЗАЛОЗИ ЗА УМОВ ВПЛИВУ СУБЛЕТАЛЬНОГО ЗНЕВОДНЕННЯ, ПОДАЛЬШОЇ РЕАДАПТАЦІЇ ТА КОРЕКЦІЇ

Ковчун В.Ю.

Зневоднення - це патологічний стан, що викликає недостатнє надходження води та супроводжується метаболічними змінами, які мають значні наслідки для здоров’я та працездатності людини. Ендокринна система приймає участь у низько функції системи обміну води, оптимізуючи об’єм та рідини організму. Літературні дослідження не завжди відбивають артеріальні зміни в умовах зневоднення і недостатньо вивчають механізми, за допомогою яких організм може адаптуватись до змін в умовах зневоднення.

Це стосується змін мікроструктури підшлункової залози. Зневоднення призводить до часткового відновлення структурних компонентів паренхіми підшлункової залози, але це патологічний стан: зміни морфоло-морфометричного складу паренхіми підшлункової залози впливають на функцію остаточних островців Лангерганса, що оптимізуючи об’єм рідини організму.

Метою дослідження було вивчення особливостей змін підшлункової залози за умов сублетального зневоднення з подальшою реадаптацією та корекцією препаратом - морфолінієвої солі тіазотної кислоти, що застосування морфолінієвої солі тіазотної кислоти здатно нормалізувати білковий, вуглеводний та ліпідний обмін. Ендокринна система приймає участь у процесах, що впливають на функцію остаточних островців Лангерганса, що оптимізуючи об’єм рідини організму.

Ключові слова: підшлункова залоза, островці Лангерганса, ацинуси, сублетальне зневоднення, морфолінієва сіль тіазотної кислоти.