INFLUENCE OF MELATONIN INTRODUCTION ON CONDITION OF THE LANGERGANS ISLETS OF THE PANCREAS IN ALLOKSAN DIABETIC RATS

INTRODUCTION ON CONDITION OF THE PANCREAS IN DIABETIC RATS

Diabetes mellitus (DM) is a common but serious metabolic disorder associated with many functional and structural complications. Diabetes is a disease that affects the millions of people every sex and race effective and globally every year [1]. Diabetes is a disease which disturbs the glycemic control and the antioxidative defence capacity, and the ensuing state of insulin beta cells, which have a particularly low antioxidative defences are ultimately responsible for the death of the beta cells, which have a particularly low antioxidative defence capacity, and the ensuing state of insulin-dependent 'alloxan diabetes'.

Melatonin not only neutralizes reactive oxygen species (ROS), but also acts through the stimulation of several antioxidative enzymatic systems and stabilizing cell membranes [3].

The object of this experimental research was to ascertain the influence of melatonin on the level of basal glycemia (BG) and histopathology of pancreatic beta-cells in rats under conditions of alloxan diabetes.

Material and methods. Research performed in compliance with the Rules of the work using experimental animals (1977) and the Council of Europe Convention on the Protection of Vertebrate Animals used in experiments and other scientific purposes (Strasbourg, 1986), according to directions of International Committee of Medical Journal Editors (ICMJE), as well as “Bioethical expertise of preclinical and other scientific researches conducted on animals” (Kyiv, 2006). The experiments were carried out on 60 sexually mature male albino rats with the body mass - (0.18-0.20) kg. Alloxan diabetes was evoked via injecting the rats with a 5% solution of alloxan monohydrate intraperitoneally in a dose of 170 mg/kg of body weight (b. w.). The animals were divided into three subgroups: 1) control group; 2) DM rats – BG≥8.0 mmol/l; 3) DM animals which were introduced the melatonin preparation intraperitoneally in a dose of 5 mg/kg of b. w. at 8 a. m. daily during 14 days starting with a 5-th 24 hour period after the injection of alloxan [4]. Haematoxylin and eosin stain and Gomori’s modified stain were used for histomorphological study of Langergans islets in pancreas [5].

Statistical analysis was performed using Statistica 10 StatSoft Inc [6]. To determine an adequate method

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of statistical estimation of the average difference between the study groups held preliminary check distribution quantities in samples. According to the criteria Shapiro-Wilk, which is used to assess the normality of distribution in the sample volume \( n \leq 50 \), all samples not received data on deviation of the distribution of samples from normal \( (p > 0.05) \). Given these data, the use of Mann-Whitney test was considered sufficient for valid conclusions. Differences were considered to be statistically significant at \( p \leq 0.05 \).

**Results and Discussion.** The blood glucose level (fig.1) of diabetic rats increased significantly throughout the experimental period. Insertion of melatonin for 14 days helped to reduce 2.0 times compared with the baseline, BG level in the group of animals with DM, indicating its hypoglycemic action.

It may be that lack of melatonin can causes impairment in glucose utilization.

It was detected, that melatonin stimulates glucose transport to skeletal muscle cells via insulin receptor substrate-1 / phosphoinositide 3-kinase (IRS-1/PI-3-kinase) pathway, which implies, at the molecular level, its role in glucose homeostasis and possibly in diabetes [7].

Histomorphological alterations (fig. 2-4) in Lang-

![Fig. 1. The level of basal glycemia (mmol/l) in blood of rats, \((n = 6, M \pm m)\): 1. a, b, c – changes are reliable \((p \leq 0.05)\). 2. a – concerning intact rats (control); b – concerning rats with diabetes mellitus; c – concerning indices on 4-th day](image1)

![Fig. 2. The pancreas of control rat. A fragment of the Langerhans islet. Gomori’s stain. Lense 40×.Eyepiece 10×](image2)

![Fig. 3. The pancreas of diabetes mellitus rat. A fragment of the Lang-erhans islet. Gomori’s stain. Lense 40×.Eyepiece 10×](image3)

![Fig. 4. The pancreas of rat with diabetes mellitus received melatonin. A fragment of the Langerhans islet. Gomori’s stain. Lense 40×.Eyepiece 10×](image4)
Melatonin could be partly due to amelioration in the oxidative stress which combat free radicals induced damages [8].

Melatonin not only neutralizes reactive oxygen species (ROS), but also acts through the stimulation of several antioxidative enzymatic systems and stabilizing cell membranes [9].

Melatonin treatment caused a sharp decrease in the elevated serum glucose and partial regeneration/proliferation of beta-cells of islets [10].

### Table

**Histomorphological changes in Langergans islets of pancreas in diabetic rats under melatonin action, (n=6, x±S**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Indexes</th>
<th>Share reliable of Langergans islets (%)</th>
<th>Numbers of betas of Langergans islets (%)</th>
<th>Percentage of beta-cells with necrosis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Control</td>
<td></td>
<td>0.946±0.0118</td>
<td>45.0±1.55</td>
<td>-</td>
</tr>
<tr>
<td>2. Diabetes mellitus</td>
<td></td>
<td>0.155±0.0128</td>
<td>5.4±0.03</td>
<td>82.0±1.95</td>
</tr>
<tr>
<td>3. Diabetes mellitus + melatonin</td>
<td></td>
<td>0.596±0.0124ab</td>
<td>58.5±1.47b</td>
<td>3.8±0.38b</td>
</tr>
</tbody>
</table>

Note: 1. a, b – changes are reliable (p≤0.05); 2. a – concerning control rats; b – concerning rats with diabetes mellitus

It is concluded that the hypoglycemic action of melatonin could be partly due to amelioration in the beta-cells of pancreatic islets.

**Conclusion.** Administration of melatonin in a dose of 5 mg/kg of body weight daily for 14 days to alloxan diabetic rats has a positive effect on the morphology of the Langerhans islets of pancreas.

**References**


**ВЛИЯНИЕ ПРИМЕНЕНИЯ МЕЛАТОНИНА НА ОСТРОВКИ ЛАНГЕРГАНСА ПОДЖЕЛУДОЧНОЙ ЖЕЛЕЗЫ КРИС С АЛЛОКСАНОВЫМ ДИАБЕТОМ**

Резюме. Целью этого экспериментального исследования было установить влияние мелатонина на уровень базальной гликемии (БГ) и гистопатологию панкреатических бета-клеток у крыс в условиях аль-
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Abstract. In the presence of intracellular thiols, especially glutathione, alloxan generates ROS in a cy-clic redox reaction with its reduction product, dialuric acid. Autoxidation of dialuric acid generates superoxide radicals, hydrogen peroxide and, in a final iron-catalysed reaction step, hydroxyl radicals. The experiments were carried out on 60 sexually mature male albino rats with the body mass – (0.18-0.20) kg. Alloxan diabetes was evoked via injecting the rats with a 5% solution of alloxan monohydrate intraperitoneally in a dose of 170 mg/kg of body weight (b. w.). The animals were divided into three subgroups: 1) control group; 2) DM rats – BG≥8.0 mmol/l; 3) DM animals which were intro-duced the melatonin preparation intraperitoneally in a dose of 5 mg/kg of b. w. at 8 a. m. daily during 14 days starting with a 5-th 24 hour period after the injection of alloxan. To determine an adequate method of statistical estimation of the average difference between the study groups held preliminary check distribution quantities in samples. According to the criteria Shapiro-Wilk, which is used to assess the normality of distribution in the sample volume n≤50, all samples not received data on deviation of the distribution of samples from normal (p>0.05). The object of this experimental research was to as-certain the influence of melatonin on the level of basal glycemia (BG) and histopathology of pancreatic beta-cells in rats under conditions of alloxan diabetes. The blood glucose level of diabetic rats increased sig-nificantly throughout the experimental period. Histomorphological alterations in Langer-gans islets of pancreas in diabetic rats were recorded: their share reliable decreased by 83 %, numbers of beta-cells decreased by 88 %, percentage of beta-cells with necrosis was 96% respectively com-pared with the indices of control animals. Melatonin treatment caused a sharp decrease in the elevated serum glucose and partial regeneration/proliferation of beta-cells of islets. It is concluded that the hy-poglycemic action of melatonin could be partly due to amelioration in the beta-cells of pancreatic is-lets.

Key words: melatonin, alloxan diabetes, pancreas.