Corrective effect of physical loads used at different times of the day in metabolic disorders (experimental study)

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Abstract
Objective of the study was to evaluate the effect of physical activity used at different times of the day on metabolic disorders in an experiment on mice with a model of type II diabetes mellitus.
Methods and structure of the study. The effect of physical activity used at different times of the day on metabolic disorders was studied in an experiment on mice with a model of type II diabetes mellitus.
Results and conclusions. It has been shown that forced physical activity in the form of daily treadmill running has a number of pronounced effects on the metabolism in mice with type II diabetes mellitus. This is manifested in a decrease in body weight, an increase in the rate of glucose uptake. All of the above indicates the normalization of carbohydrate metabolism under the influence of regular physical activity and the involution of changes characteristic of type II diabetes mellitus. It is also important that the physical effects depend on the time of day. A greater effect is the use of activity during the period of the day when the animals are passive (daylight hours), as well as shift training. The results obtained reveal a promising way of influencing metabolic processes, which is very important for finding new ways to correct metabolic disorders in type II diabetes mellitus.

Keywords: *running exercises, diabetes, obesity.*

Introduction. Health-improving physical education classes are the prevention of many diseases and the maintenance of the functioning of body systems at the proper level. In particular, it has been shown that physical activity has a positive effect on metabolic disorders [5]. Exercise increases insulin sensitivity and improves glucose tolerance [6]. It has also been shown that circadian rhythms affect the effect of exercise. The smallest change in homeostasis was recorded during training in the morning [1], the change in blood pressure also depends on what time of day the exercises were performed [2]. In addition, disruption of circadian rhythms is one of the causes of insulin resistance [3].

Objective of the study was to evaluate the effect of physical activity used at different times of the day on metabolic disorders in an experiment on mice with a model of type II diabetes mellitus.

Methods and structure of the study. Four-week-old male mice of the C57bl/6 line were used as the object of the study. Animal keeping mode: day/night: 12/12 hours, daylight hours start at 6 am, free access to food and water, room temperature 24°C.

The experiment lasted 16 weeks. Until week 12, mice were divided into two subgroups:

- animals on a fat diet - 28 mice.
- animals receiving a standard diet - 28 mice.

To form a model of type II diabetes mellitus (DM II), a high-fat diet for 12 weeks, designed specifically for this experiment, was used. The composition and energy value of the feed are described in detail in our previous work [4].

Starting from the 12th week, each group of animals was divided into two subgroups - subjected (main - 21 animals) and not subjected (control - 7 animals) to running loads.

Different subgroups of mice of the main group were subjected to a running load at different times of the day.

Group A - exposed to running load during daylight hours (from 8-00 to 10-00 hours) - 7 animals;

Group B - subjected to running load in the dark (from 19-00 to 21-00 hours) - 7 animals;

Group C - the time of the running load alternated (shift training): the first and third weeks in the dark (from 19-00 to 21-00), the second and fourth weeks - in the daytime (from 8-00 to 10-00 hours) - 7 animals.

For exercise, a BMELABSID-TM10 mouse treadmill was used [7]. The compulsion to run was carried out by electrical stimulation.

Forced running loads were carried out for four weeks. Six times a week, the duration of the load gradually increased during the first six days from 10 to 60 minutes (an increase of 10 minutes per day) and did not change again over the next three weeks. Every week we changed the angle of elevation of the treadmill (from 0 to 10°) and the speed of its rotation (from 15 to 18 m/min). Once a week, the load was not performed (on the seventh day).

Body weight was measured using laboratory scales. Blood glucose concentration was measured using a portable glucometer PKG-02.4 Satellite Plus (OOO ELTA Company, Russia). Blood samples were obtained by puncture of the tail vein.

Data are presented as mean ± error of mean. After checking the normal distribution of the data using the Kolmogorov-Smirnov test, the characteristics were analyzed using two-way analysis of variance by Kruskal-Wallis or Friedman. Statistical processing of the results was carried out using the Graph Pad Prism software package.

Results of the study and their discussion. As a result of the use of a fat diet in mice, the formation of excess body weight was revealed. Statistically significant differences with the control group in terms of weight are observed from the seventh week ($p=0.02$), by the 16th week the difference approaches 100% ($p<0.001$).

At week 12, the mice began to exercise on the treadmill. Mice fed a fat diet and exercised began to lose weight compared to mice that were not exercised. At week 13 the difference was 4%, at week 16 it was 19% (7.2 g). The body weight of mice in the control groups with loads and without loads on the 12th week differed by 2%, by the end of the experiment it began to differ by 3%. Both groups had normal body weight for this age. At the 16th week of training, a significant decrease in body weight was observed in all groups of exercising mice.

It is important to note certain differences in the effects of physical activity applied at different times of the day. A significant decrease in body weight was noted after two weeks of using a shift mode of physical activity. The use of loads in the light and dark phases led to a decrease in body weight later, only after 4 weeks, while reaching the same values as in the shift mode.

All animals periodically underwent a glucose tolerance test (GTT). In the first week of the experiment, the maximum blood glucose level was reached at around 15 minutes and amounted to 12.35 mmol/l in the control group and 14.2 mmol/l in the experimental group. At the 30th minute, the glucose level was lower than at the 15th minute, and by the 120th minute it reached values close to the initial level.

By the 8th week of the experiment, the degree of glucose uptake decreased in the experimental group. In 15 minutes after the carbohydrate load in mice of the experimental group, the level of glucose in the blood reached a maximum - 123% of the initial value. After 30 minutes, blood glucose levels began to decline, dropping to 93% of baseline. In the control group, the glucose index reached its maximum by 30 minutes, and by 120 minutes it was 12% higher than the initial value, in contrast to the glucose index at 120 minutes in the experimental group - 22% of the fasting index.

By week 16, the rate of glucose uptake in non-exercised mice increased compared to mice fed a fat diet and forced running. After 60 minutes, the blood glucose level in the trained mice decreased to 14.46 mmol/l, while in the untrained mice the glucose concentration remained at 17 mmol/l. By the 120th minute, in mice subjected to exercise, the blood glucose level approached the initial value (6.92 mmol/l) and amounted to 8.35 mmol/l. In the non-exercise group, this difference was 45%. Physical activity largely (but not completely) eliminated these disorders.

The hypoglycemic phase indirectly reflects the rate of insulin production and tissue sensitivity to this hormone. The prolongation of this phase is characteristic of type II diabetes mellitus, which was observed in mice of the experimental group in this study.

In mice of the control group, the maximum increase in glucose concentration was observed at the 30th minute and amounted to 15.46 mmol/l (137% of the norm on an empty stomach). Then the blood glucose level begins to decrease (hypoglycemic phase) and by the end of the second hour of observation (by the 120th minute) approaches the initial level in the control group (7.94 mmol/l). In mice subjected to exercise, the hypoglycemic phase begins even earlier - at the 15th minute, the glucose level begins to decrease and by the 120th minute drops to a level of 7.11 mmol/l (17% of the fasting value).

Conclusions. It has been shown that forced physical activity in the form of daily treadmill running has a number of pronounced effects on the metabolism in mice with type II diabetes mellitus. This is manifested in a decrease in body weight, an increase in the rate of glucose uptake. All of the above indicates the normalization of carbohydrate metabolism under the influence of regular physical activity and the involution of changes characteristic of type II diabetes mellitus. It is also important that the physical effects depend on the time of day. A greater effect is the use of activity during the period of the day when the animals are passive (daylight hours), as well as shift training.

The results obtained reveal a promising way of influencing metabolic processes, which is very important for finding new ways to correct metabolic disorders in type II diabetes mellitus.

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