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**Interval Hypoxic Training in Rehabilitation Program for Adolescents with Overweight / Obesity and Comorbid Arterial Hypertension: Open-Label Randomized Study**

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***Background****. Searching for new strategies for the rehabilitation of adolescents with obesity and comorbid arterial hypertension (AHT) before significant pathological changes development in the cardiovascular system remains the urgent challenge.* ***Objective.*** *The aim of the study was**to examine the effect of interval hypoxic training (IHT) on blood pressure (BP) levels in adolescents with overweight/obesity and comorbid AHT.* ***Methods.*** *Adolescents aged 14–17 years with body mass index SDS ≥ 1 and grade I AHT (mean level of systolic and/or diastolic BP ≥ 95th percentile for population of corresponding age, sex and height) have been randomized to the group "aerobic training" (treadmill walking) and “aerobic training + IHT” (usage of hypoxicator in intermittent operation cycles). All patients were on subcaloric diet (10% reduction in caloric intake for given age). Primary outcome measure was the difference between groups on systolic / diastolic BP levels according to 24-hour BP monitoring after completion of training program (10 classes each). The effects of IHT on body composition (bioelectrical impedance analysis), heart rate variability and psychoemotional state (Spielberger scale, assessment of health, activity and mood) were further estimated.* ***Results.*** *43 patients were assigned to the index group, and 42 — to the control group. 67 patients have completed the research program. 5 patients (12%) from the IHT group and 13 patients (31%; p = 0.029) from the control group prematurely discontinued participation in the trial due to poor exercise tolerance. The groups were comparable in baseline systolic and diastolic BP. Decrease in BP occurred in both groups after 10 workouts. There were no differences in decrease value: mean difference for SBP was 2.4 mm Hg (95% CI –6.6... 1.8), for DBP — 0.2 mm Hg (−3.6... 4.0). However, the incidence of reaching the targeted SBP (<95th percentile for the corresponding age and sex) after completion of the treatment was recorded in 66% patients in the experimental group and in 42% patients in the control group (p = 0,047). Positive dynamics in several indicators of heart rate variability and psychoemotional state were mentioned in the IHT group.* ***Conclusion.*** *The IHT implementation in the complex of rehabilitation program for adolescents with overweight / obesity and AHT has no additional positive effect on BP levels. However, the incidence of reaching the targeted SBP (<95th percentile for the corresponding age and sex) after completion of the treatment was recorded in 66% patients in the experimental group and in 42% patients in the control group (p = 0,047).*

***Key words:*** *adolescents, obesity, arterial hypertension, aerobic exercise, interval hypoxic training*

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**RESULTS**

**Table 1.** Baseline characteristics of patients from index and control groups

|  |  |  |  |
| --- | --- | --- | --- |
| **Indexes** | **Index group, *n* = 43** | **Control group, *n* = 42** | ***р*\*** |
| Gender (female), abs. (%)  | 16 (37) | 17 (40) | 0,758 |
| Age, years | 16 (15; 17) | 16 (1,5; 16) | 0,895 |
| Height, cm | 166,1 ± 10,2 | 168,3 ± 9,4 | 0,375 |
| Height SDS  | 0,8 (−0,03; 1,3) | 0,6 (−0,01; 1,0) | 0,248 |
| Weight, kg | 67,7 (60,0; 82,8) | 78,0 (71,6; 86,3) | 0,002 |
| BMI, kg/m2 | 25,2 (24,4; 27,2) | 28,2 (27,0; 28,9) | 0,001 |

*Note*. Here and in Tables 2–5: index group — patients randomized in IHT group (hypoxic training + rehabilitation exercises), control group — rehabilitation exercises only; <\*> — comparison of quantitative values with nonparametric value distribution (age, weight, BMI) was performed with Mann–Whitney test, with parametric distribution (height, height SDS) — Student's *t*-testfor independent samples.

**Table 2.** SBP / DBP dynamics as a result of training

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Indexes** | **Time range** | **Index group** | **Control group** | ***р*** |
| SBP, mm Hg | initially (*n* = 43/42)\* | 131,7 ± 7,7 | 131,4 ± 9,8 | 0,902 |
| initially (*n* = 38/29)\*\* | 130,8 ± 7,8 | 130,5 ± 10,3 | 0,917 |
| after treatment (*n* = 38/29) | 119,6 ± 9,0 | 122,0 ± 7,7 | 0,279 |
| difference\*\*\* | −2,4 (−6,6 … 1,8) |  |
| DBP, mm Hg | initially (*n* = 43/42)\* | 71,9 ± 3,6 | 72,9 ± 4,1 | 0,252 |
| initially (*n* = 38/29)\*\* | 72,1 ± 3,2 | 73,6 ± 3,6 | 0,515 |
| after treatment (*n* = 38/29) | 72,9 ± 7,8 | 72,7 ± 7,3 | 0,919 |
| difference\*\*\* | 0,2 (−3,6 … 4,0) |  |

*Note*. Here and in Tables 3–5: description of quantitative values in groups was performed with indication of arithmetic mean and стандартного отклонения or median (25th; 75th percentiles); <\*> —initial values in patients included in the study; <\*\*> — initial values in per-protocol patients; <\*\*\*> — difference in last (after 10th training) values between groups with indication of arithmetic mean or median and 95% CI.

**Table 3.** Change in BMI SDS and body composition due to trainings

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Indexes** | **Time range** | **Index group** | **Control group** | ***р*** |
| BMI SDS | initially (*n* = 43/42) | 1,9 (1,5;2,2) | 2,0 (1,8;2,2) | 0,223 |
| initially (*n* = 38/29) | 1,8 (1,4;2,1) | 1,9 (1,9;2,2) | 0,020 |
| after treatment (*n* = 38/29)\* | 1,8 (1,3;2,0) | 1,9 (1,8;2,1) | 0,016 |
| difference\*\* | −0,32(−0,56 … −0,06) |  |
| Fat tissue in general body weight, % | initially (*n* = 43/42) | 32,5 ± 6,0 | 33,4 ± 6,9 | 0,594 |
| initially (*n* = 38/29) | 32,9 ± 3,7 | 34,2 ± 6,6 | 0,471 |
| after treatment (n=38/29) | 31,9 ± 3,7 | 34,1 ± 6,5 | 0,217 |
| difference | −2,2 (−5,6 … 1,4) |  |
| Water in general body weight, % | initially (*n* = 43/42) | 49,5 ± 3,9 | 50,9 ± 6,8 | 0,327 |
| initially (*n* = 38/29) | 48,6 ± 3,3 | 51,0 ± 6,9 | 0,213 |
| after treatment (*n* = 38/29) | 47,0 ± 2,7 | 46,0 ± 8,0 | 0,645 |
| difference | 1,0 (−2,9 …5,1) |  |

**Table 4.** Change in ВСР values due to trainings

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Indexes** | **Time range** | **Index group** | **Control group** | ***р*** |
| LF | initially (*n* = 43/42) | 866 (501;1689) | 1349 (882;3311) | 0,008 |
| initially (*n* = 38/29) | 821 (446; 1804) | 1330 (740; 2543) | 0,060 |
| after treatment (*n* = 38/29) | 975 (693; 2513) | 645 (329; 1264) | 0,025 |
| difference | 471(76 … 1215) |  |
| HF | initially (*n* = 43/42) | 294 (135;562) | 272 (129;754) | 0,725 |
| initially | 274 (115; 420) | 327 (135; 875) | 0,196 |
| after treatment (n = 38/29) | 359 (140; 679) | 213 (78; 300) | 0,045 |
| difference | 135(2 … 350) |  |
| LF/HF | initially (*n* = 43/42) | 3,3 (2,0;5,8) | 4,2 (2,3;5,8) | 0,822 |
| initially (*n* = 38/29) | 3,4 (2,4; 6,3) | 4,2 (2,4; 6,4) | 0,992 |
| after treatment (n = 38/29) | 4,0 (2,0; 7,8) | 4,5 (2,8; 10,0) | 0,678 |
| difference | −0,5(−3,2 … 1,6) |  |
| RRmin | initially (*n* = 43/42) | 491 (421;563) | 492 (445;548) | 0,968 |
| initially (*n* = 38/29) | 491 (421;563) | 524 (450;548) | 0,649 |
| after treatment (*n* = 38/29) | 478 (406;516) | 474 (424;516) | 0,874 |
| difference | −2(−64 … 45) |  |
| RRmax | initially (*n* = 43/42) | 773 (677;923) | 784 (691;899) | 0,734 |
| initially (*n* = 38/29) | 744 (675;844) | 844 (779;953) | 0,031 |
| after treatment (*n* = 38/29) | 794 (701;935) | 748 (620;852) | 0,196 |
| difference | 62,5(−36 … 171) |  |
| Coefficient 30/15 | initially (*n* = 43/42) | 1,2 (1,1;1,4) | 1,5 (1,3;1,6) | 0,004 |
| initially (*n* = 38/29) | 1,2 (1,1;1,4) | 1,5 (1,3;1,6) | 0,003 |
| after treatment (*n* = 38/29) | 1,3 (1,2;1,6) | 1,2 (1,1;1,4) | 0,030 |
| difference | 0,15(0,02 … 0,27) |  |
| Heart rate increase, % | initially (*n* = 43/42) | 38,2 (31,0;49,1) | 35,8 (27,8;51,8) | 0,576 |
| initially (*n* = 38/29) | 40,9 (32,0;51,0) | 31,8 (23,5;36,2) | 0,002 |
| after treatment (*n* = 38/29) | 36,4 (31,8;46,4) | 45,1 (23,3;56,6) | 0,248 |
| difference | −6,3(−16 … 7;5) |  |

**Table 5.** Results of psychodiagnostic examination initially and after completion of training cycle

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Indexes** | **Time range** | **Index group** | **Control group** | ***р*** |
| **Health, activity and mood test** |
| Health | initially (*n* = 43/42) | 3,9 (3,8;4,0) | 3,9 (3,8;4,5) | 0,407 |
| initially (*n* = 38/29) | 3,9 (3,8; 3,9) | 3,9 (3,8; 4,1) | 0,337 |
| after treatment (*n* = 38/29) | 4,2 (4,2; 5,4) | 4,0 (3,9; 4,2) | 0,001 |
| difference | 0,35 (0,2 … 0,8) |  |
| Activity | initially (*n* = 43/42) | 4,1 (4,0;4,2) | 4,1 (4,1;4,3) | 0,433 |
| initially (*n* = 38/29) | 4,1 (4,0; 4,2) | 4,1 (4,1; 4,2) | 0,704 |
| after treatment (*n* = 38/29) | 4,3 (4,0; 4,6) | 4,2 (4,1; 4,3) | 0,826 |
| difference | 0 (−0,2 … 0,4) |  |
| Mood | initially (*n* = 43/42) | 3,7 (3,6;4,2) | 3,8 (3,7;4,6) | 0,170 |
| initially (*n* = 38/29) | 3,7 (3,6; 3,9) | 3,8 (3,7; 4,2) | 0,337 |
| after treatment (*n* = 38/29) | 4,6 (4,5; 5,3) | 3,9 (3,7; 4,6) | 0,003 |
| difference | 0,8(0,6 … 1,3) |  |
| **Spielberger scale** |
| State anxiety | initially (*n* = 43/42) | 60 (40;64) | 51 (37;60) | 0,172 |
| initially (*n* = 38/29) | 60 (60;64) | 52 (31;64) | 0,107 |
| after treatment (*n* = 38/29) | 45 (44;48) | 48 (40;56) | 0,155 |
| difference | −4(−10 … 3) |  |
| Trait anxiety | initially (*n* = 43/42) | 55 (45;56) | 55 (45;55) | 0,533 |
| initially (*n* = 38/29) | 55 (55;56) | 55 (45;55) | 0,143 |
| after treatment (*n* = 38/29) | 55 (53;56) | 55 (45;55) | 0,202 |
| difference | 1(0 … 10) |  |

**STUDY LIMITATIONS**

***Sample representativeness***

The small sample size in this study does not allow to extrapolate confidently the results onto the general population — all children with AHT and overweight / obesity. The study results should be extrapolated carefully to other children age groups due to possible differences in the response to IHT.

***Sample size***

The required sample size was not determined on the study planning stage. Samples sizes in studies that examined the hypotensive effect of IHT varied between 30–60 patients in each group [14, 17]. Moreover, the sample size of our study was limited due to exclusion of several participants from the analysis because they did not complete the study protocol (18 out of 85, or 21% of participants). We think that control group patients' refusal to continue the treatment could be associated to poor exercise tolerance. It has been shown in clinical and experimental studies that modeling of mountain conditions (IHT) activates adaptive responses such as increase in exercise tolerance [14, 34]. Maximal pulmonary breathing capacity increases, erythrocytes and hemoglobin concentrations increase (due to pool output), blood vessels dilate, vascular wall stiffness decreases in response for oxygen concentration decrease in inhaled air [14, 35]. These physiological adaptive reactions, in our opinion, predetermined the greater resistance of patients from the index group to the used load. Moreover, patients from the index group and/or their legal representatives were additionally informed about the possible benefits of IHT, so it also could be the reason for their higher adherence to the study protocol. It is not inconceivable that the more frequent refusal of the control group patients to continue the participation in the study was associated with the activation of autonomic nervous system (ANS) that did not allow to cope with exercises [36]. On the other hand, in the index group, there was the increase in high-frequency range waves characterizing parasympathetic activity processes as the result of training [18, 28]. It can probably reflect to decrease in ANS sympathetic activity. Therewith, patients from the index group had better levels of health and mood (according to health, activity and mood test) after completion of training. It is important for motivation and continuation of rehabilitation on the outpatient basis.

***Groups baseline comparability***

Patients from the control group had bigger weight and BMI after randomization. Adolescents in this group may experience significant difficulties in performing recommended exercises. The higher is BMI, the more frequent are complaints on poor exercise tolerance [8–10]. This factor could be the reason for the relatively low efficacy of the training program for the control group adolescents.

***Other limitations***

The absence of follow-up observation also can be the limitation of this study. It does not allow to estimate the persistence of the obtained effect. The question of whether the hypoxia training regimen will lead to long-term outcomes requires further studies. Moreover, this work did not estimate such physiological effects of IHT as carbohydrate, lipid, protein and mineral metabolism, as it was demonstrated in the study of IHT in adult patients with obesity and metabolic disorders [11–13].

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**CONFLICT OF INTERESTS**

Not declared.