Original paper

Reduction of sitting time has a positive effect on the decrease of insulin resistance in patients with non-alcoholic fatty liver disease

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Abstract

Introduction: Non-alcoholic fatty liver disease (NAFLD) affects a large part of the human population. One of the major environmental factors associated with the risk of NAFLD is the lack of physical activity.

Aim: To compare the level of physical activity and the insulin resistance in NAFLD patients.

Material and methods: Thirty patients with NAFLD underwent a six-month dietary intervention based on the principles of classical dietetics. Data about diet and physical activity was based on 72-hour nutrition diaries and International Physical Activity Questionnaire (IPAQ). Standard blood biochemical analyses were carried out before and after diet at the University Hospital Laboratory.

Results: The study showed that total physical activity and physical activity in leisure time are negatively correlated with insulin resistance (HOMA-IR) ($p < 0.05$). Insulin ($p < 0.05$), body weight ($p < 0.05$), and waist-hip ratio (WHR) ($p < 0.05$) were also negatively correlated with physical activity in free time. In addition, we noticed a positive correlation between sitting time and the risk of insulin resistance, in the case of HOMA-IR and insulin concentration ($p < 0.05$).

Conclusions: Dietary intervention and a physical activity plan are important factors in the treatment of non-alcoholic fatty liver disease. Taking regular exercise increases insulin sensitivity and prevents further development of the disease. It seems that diet and physical activity are not the only one risk factors of NAFLD. Our study reveals that the reduction of sitting time has a positive effect on the level of insulin and it reduces insulin resistance in patients with NAFLD.

Introduction

Non-alcoholic fatty liver disease (NAFLD) affects a large part of the human population. It is estimated that the incidence of the disease, depending on the country, is 10–24%. When it comes to obese people, NAFLD will develop among 57.5–74% of cases in the population [1, 2]. The crucial factors in the development of NAFLD are: hyperinsulinaemia, insulin resistance, increased lipolysis of peripheral tissues, oxidative stress, and the accumulation of triglycerides (TG) in hepatocytes.

One of the major environmental factors associated with the risk of NAFLD is the lack of physical activity. It results in a positive energy balance. The balance is the main cause of obesity and it leads to insulin resistance [3]. The cells lose their sensitivity to insulin, which is reflected in increased gluconeogenesis and hyperglycaemia. On the other hand, the insulin resistance may result in increased insulin secretion and hyperinsulinaemia. High levels of the hormone stimulate hepatic synthesis of fatty acids and leads to steatosis [4, 5]. Insulin sensitivity can be achieved mainly through appropriate diet and physical activity.

Physical activity reduces insulin resistance, regardless of weight reduction. Population studies show that 43–87% of adult Europeans do physical activity, but it is irregular. Regularity of exercise is essential for the prevention of civilisation diseases. In the case of a preventative role, moderate physical activity should last at least 30 min or 10,000 steps per day. The same result can be achieved with intense exercise three times a week for 20 min [6].

Aim

The aim of the study was to compare the level of physical activity and the insulin resistance in NAFLD patients.

Material and methods

Patients

Thirty patients with non-alcoholic fatty liver disease were enrolled in the study.

Liver steatosis was assessed by ultrasound (Acuson X300) according to the Hamaguchi score [7]. All patients had negative history of alcohol consumption (less than 20 g of pure alcohol/day). The study group underwent a 6-month dietary intervention based on the principles of classical dietetics. The diet was created using DIETETYK 6.0 software (Jumar, Poland). Data about diet and physical activity was based on 72-hour nutrition diaries and the international physical activity questionnaire (IPAQ). The study protocol was approved by the Ethics Committee of Pomeranian Medical University and conformed to the ethical guidelines of the 1975 Declaration of Helsinki.

Study plan

Study plan was presented in Figure 1.

Diet

The diet was matched to the individual calorie needs of each patient. Nutrition intervention helped to permit the reduction of body weight in overweight and obese people and allowed us to control and stabilise diabetes and dyslipidaemia. Protein intake was 1.0 g/kg body weight/day. Most proteins came from dairy products and fish. Dietary fibre was at 25–30%. Vitamin and mineral intake was provided by the appropriate amount of vegetables and fruit. Special attention was paid to the supply of vitamins, which plays a key role in the proper functioning of hepatic enzymes (vitamins A, K, C, and B). Sodium intake was limited to 5 g/day. Energy from fat ranged from 20% to 35% of the total energy intake (E). Recommended dietary fats such as cream, milk, butter, and vegetable oils were easily digestible. The energy derived from carbohydrates ranged from 50% to 65% of E.

Diet control

The patients were asked to take home and complete a 72-hour food diary (with 1 free day). The dietary records were validated by a nutritionist. The diet diary booklet contained menus, pages to record foods, and photographs of food that depicted portion choices for a common food item. The dietician reminded the patients to record the food brand and portion size. The amounts consumed were recorded in household units by volume or by measuring with a ruler.

Anthropometric measurements

During the study, anthropometric (anthropometric callipers, tape measure) and tissue bioimpedance measurements (Akern BIA) were performed. The analysis of resting metabolism rate was made using Fitmate Pro from the Cosmed system (Italy). Anthropometric parameters were analysed as follows: weight (medical

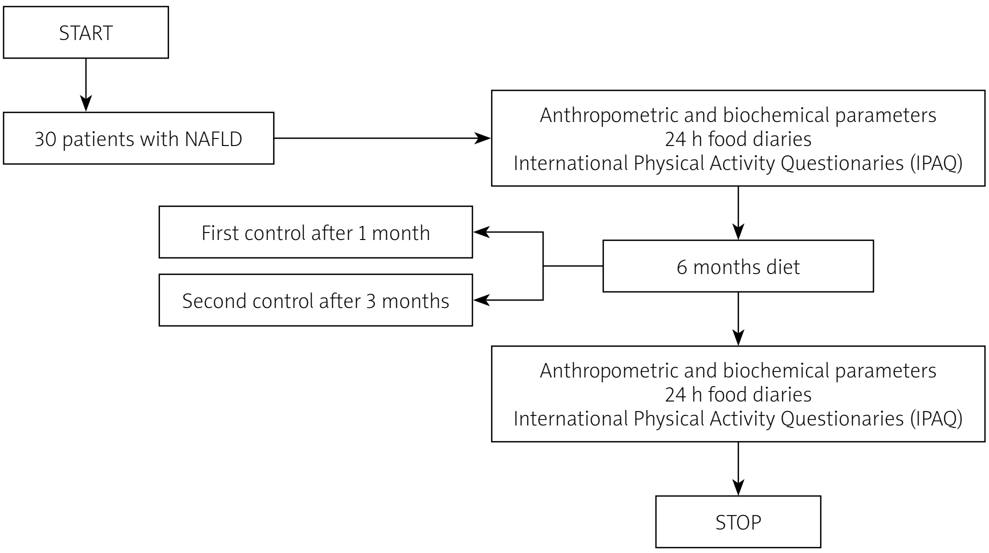

Figure 1. Study plan

weight, Radwag WPT 100/200 OW), body height (medical weight, Radwag WPT model 100/200 OW), arm circumference, waist circumference, hip circumference (tape measure), and the amount of body fat (anthropometric compasses, bioimpedance device Akern BIA). Body mass index (BMI) was calculated according to the formula: BMI = body weight [kg]/height [m^2].

Physical Activity Questionnaire

The level of physical activity was assessed using the questionnaire technique with validated International Physical Activity Questionnaire (IPAQ) [8]. Physical exercise was estimated with MET units (min/week). The patients were classified into appropriate activity categories: below 600 MET for low, 600–1500 or 600–3000 MET for moderate, and higher than 1500 or 3000 MET (min/week) for high activity.

Insulin and glucose content measurements

Whole blood was collected into ethylenediaminetetraacetic acid (EDTA) tubes. The blood was immediately placed on ice or in a refrigerator until standard blood biochemical analyses were carried out at the University Hospital Laboratory.

Statistical analysis

Statistical analysis was performed using Statistica 7.1 software. As the distribution in most cases deviated from normal (Shapiro-Wilk test), non-parametric Mann-Whitney test was used for comparisons between groups, and $p < 0.05$ was considered statistically significant. The data obtained in the study is shown by the mean and standard deviation. Spearman test was used to reveal the correlation between data.

Results

During the 6-month dietary intervention patients reported significant changes in anthropometric parameters. A reduction of the following parameters was noticed: BMI (from 30.84 ±4.33 kg/m^2 to 28.99 ±3.95 kg/m^2), fat mass (from 33.91 ±10.25 kg to 30.14 ±8.65 kg), fat tissue (from 37.62 ±8.26 to 35.15 ±8.18%), lean body mass (from 55.58 ±10.48 to 52.24 ±12.69 kg), and body water content (from 41.28 ±7.12 to 40.47 ±7.08%). The results are presented in Table I.

The analysis of physical activity questionnaires showed significant changes in the level of intensity and type of physical activity performed by the patients. According to the study, physical activity at work was strongly limited in each of the analysed aspects: walking (from 1920.6 ±1379.71 to 2114.18 ±1558.04), moderate activity (from 2612.5 ±2147.87 to 1158.46 ±1762.77), intense activity (from 2325.71 ±3432.04 to 2160 ±3702.40), and the total activity at work (from 4124.313 ±5436.01 to 2187.8 ±3977.36) (Table II).

A significant decrease in physical activity was also observed in the case of activity associated with movement: walking (from 1413.75 ±1387.01 to 828.85 ±949.63), cycling (from 1110 ±946.78 to 557.143 ±916.98), and total transport (from 1184 75 ±1599.16 to 1300.10 ±958.85) (Table III).

Table I. Anthropometric characteristics of the study group

Anthropometric feature	Before diet Mean ± SD	After 6-month diet Mean ± SD	*P*-value
WHR	0.99 ±0.06	0.94 ±0.06	< 0.05
BMI [kg/m^2]	30.84 ±4.33	28.99 ±3.95	< 0.05
Fat mass [kg]	33.91 ±10.25	30.14 ±8.65	< 0.05
Fat tissue [%]	37.62 ±8.26	35.15 ±8.18	< 0.05
Lean body mass [kg]	55.58 ±10.48	52.24 ±12.69	< 0.05
Water [%]	41.28 ±7.12	40.47 ±7.08	< 0.05

Table II. Physical activity at work

Parameter	Before diet Mean ± SD	After 6-month diet Mean ± SD	*P*-value
Walking [MET, min/week]	1920.6 ±2114.18	1379.71 ±1558.04	< 0.05
Moderate physical activity [MET, min/week]	2612.5 ±2147.87	1158.46 ±1762.77	< 0.05
Intense physical activity [MET, min/week]	2325.71 ±3432.04	2160 ±3702.40	< 0.05
Total physical activity at work [MET, min/week]	4124.313 ±5436.01	2187.8 ±3977.36	< 0.05

Table III. Physical activity during transport

Parameter	Before diet Mean ± SD	After 6-month diet Mean ± SD	*P*-value
Walking [MET, min/week]	1413.75 ±1387.01	828.85 ±949.63	< 0.05
Cycling [MET, min/week]	1110 ±946.78	557.143 ±916.98	< 0.05
Total transport [MET, min/week]	1184.75 ±1599.16	958.85 ±1300.10	< 0.05

Table IV. Physical activity at home

Parameter	Before diet Mean ± SD	After 6-month diet Mean ± SD	*P*-value
Intense physical activity around home [MET, min/week]	1891.61 ±2888.10	1272.86 ±1366.33	< 0.05
Moderate physical activity around home [MET, min/week]	1278.75 ±1241.39	871.11 ±1498.50	< 0.05
Moderate physical activity at home [MET, min/week]	671.67 ±840.85	672.22 ±668.56	NS
Total physical activity at home [MET, min/week]	2169.25 ±3021.08	1163.33 ±1594.41	< 0.05

Table V. Physical activity in free time

Parameter	Before diet Mean ± SD	After 6-month diet Mean ± SD	*P*-value
Walking [MET, min/week]	443.44 ±339.96	891 ±991.04	< 0.05
Moderate physical activity [MET, min/week]	180 ±84.85	244 ±210.57	< 0.05
Intense physical activity [MET, min/week]	1248 ±1204.79	1736.67 ±3367.63	< 0.05
Total physical activity in free time [MET, min/week]	456.5 ±728.14	1310.6 ±2258.26	< 0.05

The analysis of the questionnaires showed a decrease in physical activity performed during housework: intensive activity around the house (from 1891.61 ±2888.10 to 1272.86 ±1366.33), moderate activity around the house (from 1278.75 ±1241.39 to 1498.50 ±871.11), and total physical activity associated with housework (from 2169.25 ±3021.08 to 1163.33 ±1594.41) (Table IV).

During leisure time patients spent significantly more time doing physical activity, especially in the case of: walking (from 443.44 ±339.96 to 991.04 ±891), moderate activity (from 180 ±244 to 84.85 ±210.57), intense activity (from 1248 ±1204.79 to 1736.67 ±3367.63 MET, min/week), and total activity in leisure time (from 456.5 ±728.14 to 1310.6 ±2258.26) (Table V).

The analysis of total moderate physical activity showed that patients limited this type of activity (from 3025.92 ±3344.52 to 1876.67 ±2242.65). We also observed an almost two-fold increase in intense activity (from 750.67 ±1904.85 to 1414.67 ±3109.86). The resultant total physical activity associated with all types of activity was reduced (from 6010.13 ±5584.89 to 5620.58 ±4855.29) (Table VI).

During the project patients spent significantly less time in a sitting position. This reduction is related to the total time spent in a sitting position (from 2606.25 ±1337.89 to 1778.59 ±1393.21), as well as the average time of sitting (from 372.321 ±191.13 to 254.09 ±199.03) (Table VII).

Table VI. Total physical activity

Parameter	Before diet Mean ± SD	After 6-month diet Mean ± SD	*P*-value
Walking [MET, min/week]	2233.55 ±2425.33	2329.25 ±2237.58	NS
Moderate physical activity [MET, min/week]	3025.92 ±3344.52	1876.67 ±2242.65	< 0.05
Intense physical activity [MET, min/week]	750.67 ±1904.85	1414.67 ±3109.86	< 0.05
Total physical activity in free time [MET, min/week]	6010.13 ±5584.89	5620.58 ±4855.29	< 0.05

Table VII. Sitting time

Parameter	Before diet Mean ± SD	After 6-month diet Mean ± SD	*P*-value
Total sitting time [min/week]	2606.25 ±1337.89	1778.59 ±1393.21	< 0.05
Average total sitting time [min/day]	372.321 ±191.13	254.09 ±199.03	< 0.05

Table VIII. Correlation between data

Comparative data	Spearman's rank correlation coefficient (rho)	*P*-value
Total activity in free time vs. WHR	–0.485342	< 0.05
Total activity in free time vs. BMI	–0.468239	< 0.05
Total activity in free time vs. insulin	–0.549815	< 0.05
Total activity in free time vs. HOMA-IR	–0.53828	< 0.05
Total activity vs. HOMA-IR	–0.442857	< 0.05
Sitting time vs. insulin	0.524603	< 0.05
Sitting time vs. HOMA-IR	0.50554	< 0.05

Spearman rank correlation test was made in order to show the correlation between the types of physical activity and insulin resistance parameters (HOMA-IR and insulin) [9, 10]. Statistically significant results are shown in the following table (Table VIII).

Discussion

In our study, total physical activity was expressed as physical activity performed at work, in free time, during housework, and during transportation. We also measured the total time spent in a sitting position.

The project involved 30 patients with NAFLD. During a 6-moths dietary intervention and increased physical activity recommendation patients improved crucial anthropometric features: waist-hip ratio, BMI, and fat mass. During the study patients decreased the levels of several physical activities, such as: home activities, transport activity, and home activity. We suggest that the reason why patients spent less time on those activities may be correlated with different seasons of the year. The project lasted for 2 years and the patients were involved during different months. However, total physical activity in free time was significantly increased. This can be caused by higher awareness in the group of involved patients. We think that the main reasons that the anthropometric features decreased were proper diet, exercise in free time, and less time spent in a sitting position. Furthermore, we found a very interesting connection between activity and insulin sensitivity parameters among our patients.

Spearman's correlation showed that the total physical activity in leisure time is negatively correlated with basic markers of insulin resistance: HOMA-IR ($p < 0.05$) and insulin ($p < 0.05$). Patients who spent their free time more actively also experienced a decrease in body weight ($p < 0.05$) as well as WHR ($p < 0.05$). In addition, we noticed a negative correlation between total physical activity and HOMA-IR ($p < 0.05$). The results show that patients who spent more time on any type of physical activity decreased the risk of developing insulin resistance, which is the main cause of NFLD progression. The influence of physical activity on improving insulin resistance was previously described. The activation of GLUT 4 protein responsible for the transmembrane transport of glucose, insulin potency increase, and the improvement of glucose tolerance are all associated with the mechanism of muscle sensitivity to insulin. The improvement of glucose tolerance occurs after a week of training. This change appears regardless of body weight [11]. Bogdanski *et al.* showed that 50 min of exercise at the level of 70–75% of maximum heart rate (HRmax) performed for seven days increases insulin sensitivity and glucose tolerance by 35%. Another study revealed that 30 min of daily exercise (70–75% HRmax) helped reduce insulin concentration in 36% of patients [12]. Pilacinski *et al.* suggested a correlation between a lack of physical activity and type I diabetes. The researchers point out that exercise increases insulin sensitivity, which has beneficial effect on the patients [13].

During the 6-month dietary intervention patients with NAFLD showed positive correlation between time spent sitting and increased risk of insulin resistance. The differences in insulin concentration ($p < 0.05$) and

HOMA-IR ($p < 0.05$) were directly proportional to the amount of the total and the average total sitting time.

Hallsworth *et al.* compared physical activity among patients suffering from NAFLD and healthy volunteers. The study showed that patients with NAFLD spent significantly more time in a sitting position. They were also more reluctant to perform intensive physical activity than the control group. The researchers point out that individuals are often unaware of how much time they spend in a sitting position and on physical activity [14]. It seems that the plan of the therapeutic treatment should include questionnaires with physical activity and sitting time. This method can be helpful in informing the patient about the risks of sedentary lifestyle. It would also allow to better monitor the progress of the therapy [15–17]. According to the American Diabetes Association, patients who suffer from metabolic syndrome, including NAFLD, should increase physical activity and adopt a well-balanced diet. Losing weight through exercise, physical activity, and caloric restriction associated with the proper diet are key elements in the struggle against dyslipidaemia and the prevention of cardiovascular disease. These actions help to reduce the LDL cholesterol fraction and blood triglycerides concentration, and increase HDL cholesterol [18–21].

Dietary intervention and a physical activity plan are important factors in the treatment of non-alcoholic fatty liver disease. Taking regular exercise increases insulin sensitivity and prevents further development of the disease. It seems that diet and physical activity are not the only risk factors of NAFLD. Our study reveals that reduction of sitting time has a positive effect on the level of insulin and the reduction of insulin resistance in patients with NAFLD.

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Conflict of interest

The authors declare no conflict of interest.

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