

ORIGINAL ARTICLE

Effects of an interdisciplinary intervention on insulin resistance indicators in overweight and obese adolescents

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Abstract

Introduction: Overweight children and adolescents are more susceptible to metabolic disorders. However, changes in lifestyle can prevent or delay the appearance of risk factors, highlighting the importance of intervening early in this population.

Objective: To analyze the effects of a six months interdisciplinary intervention program on the indicators of insulin resistance and uric acid levels in overweight and obese students.

Methods: This is an interventional study in overweight adolescents, composed of a control group (n=19) and an intervention group (n=20). The group participated in a six-month program with nutritional, psychological and physical exercise intervention, three times a week. The values of waist circumference, glucose, insulin, uric acid assessment and HOMA-IR index, were evaluated before and after the program.

Results: After 6 months, the intervention group had a significant reduction in waist circumference (p=0.007), HOMA-IR index (p=0.048) and uric acid (p=0.036); the control group did not present differences in the pre and post evaluation.

Conclusion: The intervention program was effective in reducing waist circumference, HOMA-IR and uric acid levels in overweight adolescents.

Keywords: obesity, insulin resistance, uric acid, adolescent, intervention studies.

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Authors summary

Why was this study done?

This study is part of a larger investigation entitled “OBESITY IN CHILDREN OF ELEMENTARY SCHOOL: AN INTERDISCIPLINARY INTERVENTION STUDY - PHASE II”, coordinated by Prof. Dr. Miria Suzana Burgos. It is also part of the Master Degree dissertation of M.^a Debora Tornquist from the Post Graduate Program in Health Promotion at the University of Santa Cruz do Sul (UNISC). After conducting several cross-sectional surveys with schoolchildren and observing their high prevalence of overweight and other risk factors, supported with scientific evidence, it was decided to carry out intervention programs with this population and evaluate their effects on health parameters, including those associated with glucose metabolism.

What did the researchers do and find?

We conducted an interdisciplinary intervention composed by nutritional, psychological and physical exercises was carried out three times a week for six months with a group of 20 overweight adolescents. Then, we analyzed the effects on waist circumference, glucose, insulin, HOMA-IR index and uric acid compared to a control group of 19 overweight adolescents who did not receive any intervention. At the end of the program, the intervention group showed a significant reduction in waist circumference, HOMA-IR index and uric acid; the control group showed no differences in the pre and post evaluation.

What do these findings mean?

The intervention program proved to be efficient in reducing waist circumference, HOMA-IR and uric acid levels of overweight adolescents. These findings demonstrate that early interventions, still in the school phase, are important and efficient tools to prevent and treat over weight and risk factors for cardiometabolic diseases that have been increasingly prevalent at an earlier stage.

INTRODUCTION

Insulin resistance (IR) and type 2 diabetes are becoming common among children and adolescents, are related to cardiometabolic risk and have been presented as a public health problem, requiring attention from the early stages of life^{1,2}.

Overweight youth are more susceptible to metabolic disorders, since the accumulation of body fat, especially in the abdominal region, generates an increase in fatty acids circulating in the bloodstream, which consequently impairs insulin signaling and leads to a reduction in sensitivity of receptors and tissue response to cellular actions that are mediated by this hormone^{1,3,4}. Elevated levels of uric acid (hyperuricemia) also have implications for the pathogenesis of obesity and have been linked to deteriorated glucose tolerance, impaired fasting glucose and type 2 diabetes⁵.

Some lifestyle changes, including weight reduction, increased levels of physical activity and changes in eating habits can prevent, or at least delay, the onset of type 2 diabetes². Thus, it is important to implement intervention programs in the lifestyle of overweight and obese adolescents, aiming at mitigating risk factors related to early IR⁴.

However, there are limited scientific literature, mainly in the Brazilian scenario that investigate the effect of interventions with interdisciplinary approach on the variables related to IR in overweight adolescents and the studies conducted worldwide have conflicting results⁶⁻¹⁸. Thus, this study aims to analyze the effects of a six month interdisciplinary intervention program on IR indicators and uric acid levels in overweight and obese adolescents.

METHODS

Interventional study, consisting of a control group and an intervention group, carried out with adolescents with overweight and obesity, in a municipality in southern Brazil. The study was approved by the Research Ethics Committee of the University of Santa Cruz do Sul, under protocol No. 357,403. The risks and benefits of this research, as well as its nature and design, were explained to the adolescents and their parents and/or guardians who signed an informed consent form.

The adolescents invited to participate were selected from the results of the cross-sectional survey “Schoolchildren’s Health - Phase III”, which evaluated students from 25 schools in the municipality. For convenience and reducing costs and expenses, the researchers invited students from schools close to the area of the University campus because the entire intervention process was carried out there. Seven schools were selected, and a total of 172 students, were invited to join the program, of them 49 agreed to participate. To complete the experimental group, an invitation was broadcast through the radio, newspapers, and social networks, and visits to other four schools in the municipality looking for adolescents interested in the program resulting in five more increasing the total to 54 students enrolled in the intervention program.

The characteristics of inclusion criteria for the intervention group were be between 10 to 17 years old; having a BMI \geq P85, according to the curve percentiles from the World Health Organization¹⁹, associated with a second obesity indicator, waist circumference (WC) or high fat percentage.; without any kind of physical limitations or contraindications to practice physical exercises; attend school in the morning and have time available to attend the intervention program on certain days and times. The intervention program excluded students who, during the course of the program, showed unavailability to attend sessions at previously established times, presented some type of contraindication, for a prolonged period, for the practice of physical activities; or who had 50% or more absences in the program.

The control group was composed of adolescents selected through the results of the research project “Schoolchildren’s health - Phase III”, with BMI \geq P85. The control and intervention groups were matched for age, sex, and anthropometric variables, for each student in the intervention group, a pair from the control group was added. The control group did not undergo any type of intervention during the program, they only underwent to a pre and a post evaluation, performed at the beginning and at end of the 6 month program.

The interdisciplinary intervention was ran from April to September 2015, with sessions three times a week on Mondays, Wednesdays, and Fridays, lasting two hours (from 2 pm to 4 pm) totaling 70 sessions. The program was also attended by physical-education professionals, psychologists, and nutritionists. The physical-exercise sessions took place in the sports complex of the University of Santa Cruz do Sul, and the psychological and nutritional sessions took place elsewhere in the university premises, including its Nutrition and Dietetics laboratory.

On Mondays, the session consisted of an hour of psychological intervention and an hour of sports class, with warm-up, stretching, pedagogical processes and game (varying the modality each week, including football, basketball, volleyball, futsal, handball, dance, Jiu-Jitsu, among others); in Wednesday's sessions, the intervention was exclusively of exercises, contemplating aerobic part (which had its duration gradually increased during the program), circuit of resisted and functional exercises, breathing exercises and postural correction; on Fridays, one hour of the session was dedicated to intervention and nutritional guidance and one hour of session in the pool, varying from activities of initiation to swimming, water aerobics, resistance, dance and recreational games. The intensity of physical exercises was monitored in all sessions, using the Polar cardiac monitor - FT1, in which the participants were instructed to maintain the heart rate (HR) in the zone of 50% to 70% of the maximum HR, calculated in the first intervention session for each subject, using the Karvonen equation, in which maximum HR = 220 - age.

The nutritional intervention emphasized the reduction of the consumption of fats, sugars, and sodium through educational activities, using various methodologies (including lectures, conversation circles, games, clippings and collages, educational materials, tasting food or drink preparations, and practical classes in the laboratory), aimed at increasing knowledge regarding these foods, risks of excessive consumption, and ways to replace them in their diet. No diet was prescribed, and goals for changing eating habits were established each week.

Psychological counseling was carried out in 13 semi-structured sessions, with an average duration of 50 minutes each, consisting of counseling and cognitive training in groups. The program followed the guideline of an individual session, using psychoeducation on the techniques approached, executing the technique worked on the day, and assigning homework. The guidance and training group focused on process for the management of thoughts related to obesity, working on cognitive methods to recognizing and restructuring dysfunctional thoughts, along with relaxation techniques.

Pre-intervention evaluations were carried out in March and post-intervention, in the last week of September, at the university's premises. WC was assessed using an inelastic measuring tape with a resolution of 1 mm (Cardiomed®), having as reference point the narrowest part of the trunk between the ribs and the iliac crest.

At the University's Exercise Biochemistry Laboratory, were done the tests of glucose, fasting

insulin, and uric acid were done by collecting blood samples, with the adolescents fasting and resting for twelve hours prior to collection. Ten mL of blood was collected in the brachial vein, of them 5 mL were transferred to a dry vacutainer tube (with a clot activator) to obtain the serum. From this glucose, insulin, and uric acid were analyzed using commercial kits from DiaSys (DiaSys Diagnostic Systems, Germany). Glucose and uric acid obtained using the automated equipment Miura One (ISE, Rome, Italy) and insulin using the Enzyme-Linked Immune Sorbent Assay (ELISA) technique. The HOMA-IR Index, expressed by the equation $HOMA-IR = \text{fasting insulin } (\mu\text{IU/mL}) \times \text{fasting glucose (mmol/mL)} / 22.5$, was calculated to assess the insulin resistance.

Statistical analyzes were performed through the SPSS 23.0 program, initially using the Shapiro-Wilk test to evaluate the normality of the variables, considering $p > 0.05$ a normal distribution. To compare the results of the pre and posttest, between the control group and the intervention group, the *t* test was used for the parametric variables for the independent samples and for descriptive analysis, the mean and standard deviation were used. For the non-parametric variables, the Mann-Whitney test was adopted, and the results of the median and interquartile ranges were used to describe the data. To compare the pre and posttests within the group, the paired samples test was used among the variables with normal distribution, and the Wilcoxon test was used among the non-parametric ones. In both tests, the level of significance was set at $p < 0.05$.

RESULTS

Of the 54 adolescents enrolled to start the intervention program, five losses occurred in the intervention group between acceptance and the first intervention session; thus, 49 subjects started the intervention process. During the six months of intervention, 26 subjects dropped out of the program or were excluded due to excessive absences, with the final intervention group consisting of 23 subjects. As for each student in the intervention group, a pair from the control group was added, the final control group is also composed of 23 subjects.

Of the 46 subjects (23 from each group), not enough blood was obtained to perform all the predicted analyzes of three individuals from the intervention group and four from the control group. Thus, the final sample was composed of 20 subjects in the intervention group, ten male and ten female, aged between 11 and 17 years (mean 13 ± 1.48) and 19 in the intervention group, 9 male and 10 female, aged 10 to 16 (mean age 12 ± 1.82 , with no difference in the intervention group, $p = 0.238$). The figure 1, illustrates step by step the sampling process.

The table 1 shows the comparison of values of pre-test and post- test between the control and intervention groups.

Table 2 shows the differences of the pre-tests and post- tests between the control and intervention groups, in which a significant reduction in waist circumference ($p = 0.007$), HOMA-IR index ($p = 0.048$) and uric acid ($p = 0.036$).

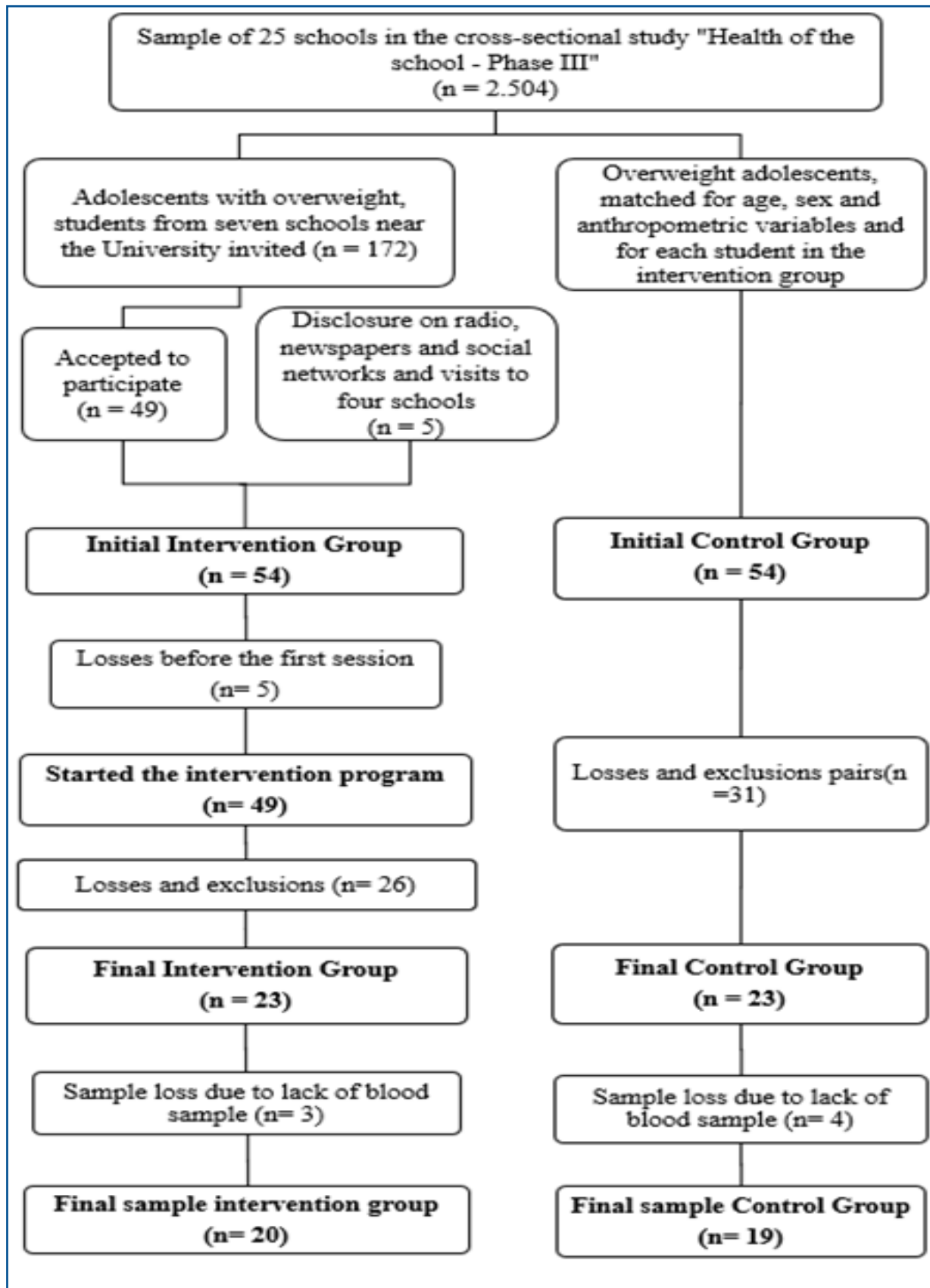


Figure1: Flow Diagram of Sampling Process

Table 1: Comparison of pre-test and post-test values between control and intervention groups of overweight adolescents from Santa Cruz do Sul – RS, Brazil, 2015

	Pre-test			Post-test		
	Control Group (n=19)	Intervention group (n=20)	p	Control Group (n=19)	Intervention group (n=20)	p
WC (cm)	81.5 (8.9)	88.0 (13.4)	0.084*	75.2 [71.4 – 84.0]	80.1 [74.2 – 86.0]	0.356**
FG (mg/dL)	89.4 (5.9)	87.7 (6.1)	0.391*	89.1 (6.7)	86.5 (7.9)	0.287*
FI (µU/ml)	10.3 [9.0 -18.3]	15.5 [9.9 – 21.0]	0.152**	12.8 [7.9 – 20.3]	13.5 [8.5 – 20.6]	0.922**
HOMA-IR	2.4 [1.9 – 4.2]	3.5 [2.1 – 4.6]	0.216**	2.9 [1.9 – 4.1]	2.8 [1.7 – 4.7]	0.978**
UA (mg/dL)	4.9 (0.9)	5.3 (1.1)	0.278*	4.5 (1.3)	4.7 (0.9)	0.618*

WC = Waist circumference; FG = Fasting glucose; FI = Fasting Insulin; UA = Uric acid.

* T test for independent samples. Results on average (± standard deviation);

** Mann-Whitney test. Results in median [interquartile ranges].

Table 2: Differences (Δ) by comparing the pre and post-intervention periods in control and intervention groups of overweight adolescents from Santa Cruz do Sul – RS, Brazil, 2015

	Group Control (n=19)		Intervention group (n=20)	
	Δ (±sd)	p	Δ (±sd)	p
WC (cm)	- 1.8 (6.8)	0.113**	- 6.0 (8.6)	0.007**
FG (mg/dL)	- 0.3 (5.9)	0.818*	-1.2 (7.5)	0.484*
FI (µU/ml)	-0.2 (5.8)	0.856**	-1.7 (4.1)	0.100**
HOMA-IR	-0.0 (1.3)	0.841**	-0.4 (0.9)	0.048**
UA (mg/dL)	-0.4 (0.9)	0.084*	-0.6 (1.1)	0.036*

WC = Waist circumference; FG = Fasting glucose; FI = Fasting Insulin; UA = Uric acid.

* t test for paired samples

** Wilcoxon test

DISCUSSION

To the best of our knowledge, this is the first study to evaluate the effects of an interdisciplinary intervention on the various variables related to IR in a population of overweight Brazilian adolescents. The results of the present study indicate a positive effect of the six months of intervention, with a reduction in WC, the HOMA-IR insulin resistance indicator, and uric acid levels. These results are relevant for formulating future programs and projects that are effective in promoting health and preventing risk factors in the population of obese youth.

However, the study has some limitations, including the inability to control the quantity and quality of food consumption by the adolescents, since, it was not possible to monitoring their habits and meals outside the intervention. Even though questionnaires were used to monitor participants' diets, the answers could easily be influenced by what individual's considered to be healthy. It is also noteworthy that, although special care was taken to ensure that sample loss was as small as possible, calls and meetings were conducted whenever significant absences were noted from any participant; the period of time and frequency of interventions scheduled caused that 50% of students left the program earlier.

During the time of the intervention a severe winter and intense rains affected the region what probably influenced in the high number of absences among the adolescents. Another point to be highlighted is the sample loss resulting from the insufficient amount of the blood

available to perform insulin analysis, especially in the individuals with obesity, whose blood it is difficult to collect. All of these factors made it impossible to perform parametric analyzes for all the variables investigated, resulting in a loss of static power.

Nevertheless, the study has some advantages, such as the pairing performed for each subject in the intervention group, which allowed the experimental and control groups to have very similar characteristics, *i.e.*, with no differences in the pre-intervention variables that could influence the results of the study. The fact of non-interference in the adolescent daily routines was important to avoid factors that could affect the results. A positive aspect of the study was its emphasis on diversified and fun physical activities, in which several types of exercises were offered, designed to provide better experiences and improved adherence to practices in the period after the intervention.

In this sense, in a study by Calcaterra *et al.*⁷, the authors emphasize that intervention programs with this population do not need to be associated with vigorous and exhaustive levels of physical activities and that recreational programs are effective in encouraging obese young people to participate. Brambilla *et al.*²⁰ point out that, in cases where physical activity is provided in supportive environments (only involving overweight young people), team sports can be a great attraction and incentive to practice.

These practices are not as successful as when practicing with normal-weight peers and can be an alternative weight-control treatment. Resistance exercises, although they may be well tolerated by young overweight people due to the fact that individuals with greater body mass are able to lift larger weights, should not be carried out in isolation, since the participants will observe very little or no weight loss as a consequence of an increase in lean mass, which could be discouraging and lead to increased program dropouts²¹.

Nevertheless, a study by Mello *et al.*²² found that mixed training, including aerobic and resistance training, is more successful in improving body composition and metabolic syndrome components. Thus, our proposal of offering diversified, fun activities involving various sports, aerobic and resistance exercises, could be crucial in attracting and maintaining the interest of obese young people and help them to achieve good health results.

The comparison of our results with the findings published in the literature should be performed with caution, as the studies found differ in the most varied methodological aspects, such as the type of interventions and active professionals, the duration and frequency of the program, types of physical exercises performed and their frequencies, time dedicated by participant, among others.

Although many variables can be used as anthropometric indicators, we chose to use WC, as this parameter is closely correlated to the BMI²³, and also provides information on abdominal fat instead of total body mass since the metabolic risk and obesity-related comorbidities are more associated with visceral fat deposits than the amount of total fat. In addition, WC, as a recommended marker of abdominal obesity, is one of the risk criteria for metabolic syndromes in children over 10 years of age, according to the International Diabetes Federation²⁴.

The reduction in WC can be considered to be a very positive effect of the intervention program, as this is indicative of the reduction of abdominal fat, an effect that is associated with an improvement in insulin resistance and, consequently, a decrease in the risk of type-2 diabetes²⁵. Other intervention studies conducted with overweight children and adolescents also found improvements in WC⁶⁻¹¹.

Regarding fasting glucose and insulin, although adolescents have lower levels after the intervention, the difference was not significant. The results of these parameters in adolescents reported in previous studies are contradictory. Some indicate a reduction in fasting glucose^{7,8,12-14}, while others do not^{10,15,16}; further, some indicate a reduction in fasting insulin^{8,9,12-15,17}, while others have not observed this effect^{7,10,16}.

The insulin resistance was assessed by HOMA-IR index instead of the gold standard recommended for children and adolescents, "the hyperinsulinemic clamp test" which is very expensive¹. In our study, the HOMA index showed a positive trend after six months of the intervention, which decreased in the group that participated in the program. This is an important result, as it is an indication that this type of intervention can improve IR at an early stage of obesity and prevent progression of the disease⁶. Furthermore, success in the treatment and

reduction of metabolic markers are important because they are crucial indicators of cardiovascular risk in the future²⁶.

The results of previous intervention studies are also conflicting regarding the HOMA-IR index, where some studies have improved this parameter^{7,8,10-15} and others have demonstrated no effects^{6,16}. The effects of physical exercise on insulin sensitivity are related to an increased uptake of glucose metabolism by the muscle, along with increased synthesis and translocation of the glucose transporter in skeletal muscle and adipose tissue, Glut-4. In addition, the adaptations of the skeletal muscle include hemodynamic effects of insulin improvement, and the training results involve changes in the expression of proteins involved in the metabolism and absorption of glucose²⁷.

The uric-acid levels showed a significant reduction after the intervention program. The decrease in these levels may be related to the reduction of blood viscosity and the effects of physical exercise, which consequently increases renal blood flow and reduces the levels of uric acid in the blood¹⁰. In a similar manner to other variables, uric acid also presents conflicting results in intervention studies, where some studies have reported the same effect^{10,11,17,18} and others have not⁶.

The divergences between the methodological variables seem to interfere in the divergent results pointed out in the interventional studies with adolescents with overweight, and it seems difficult to discuss what is the best methodology used in face of different combinations of methods, types of interventions, professionals, duration and frequency of program, types, durations and intensities of physical exercises performed to show improvements in different parameters.

A systematic review of 64 interventional studies with children and adolescents to evaluate the effectiveness of the programs, concluded that interventions with physical education professionals, nutritionists and psychologists have been widely used with interdisciplinary approach and have been useful. As it seeks to intervene in the energy balance, by reducing sedentary behavior by increasing physical activities and improving eating habits. Psychologist interventions are an important complementary part, as they improve the achievement of results through the identification and modification of aversive thought patterns and mood, and also help adolescents to maintain the behaviors and results achieved over time. Meta-analyzes indicated an improvement in parameters with 6 and 12 months of follow-up²⁶.

The results of our research are relevant to the point that they demonstrate the positive effects of this type of intervention regarding the reduction in abdominal obesity, which is a key cardiovascular risk factor. Further, it reduces IR, which is an important factor in preventing type-2 diabetes, and uric-acid levels, preventing hyperuricemia. Thus, our findings encourage the implementation of intervention programs, not only with adolescents who are already overweight, but also with those who are not yet, as a strategy to prevent obesity and its comorbidities. In this sense, intervention studies implemented in schools have demonstrated positive results on health and improvements in the physical activity of students^{4,28}.

In conclusion, six months of an interdisciplinary-intervention program with the participation of a physical-education professional, psychologist, and nutritionist led to a reduction in waist circumference, HOMA-IR index, and uric-acid levels in overweight adolescents.

The results and the methodological aspects of our study can assist in the planning of actions, aiming to promote changes in lifestyle and motivate physical activity in the young population with overweight, with early improvement of their health parameters to prevent the progression of risk factors.

It is recommended to conduct further studies with the population of Brazilian overweight adolescents, using similar methodological aspects, with better measures to mitigate the sample losses to ensure comparability parameters among the studies and confirm the results found.

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Author Contributions

Each author contributed individually and significantly to the development of the manuscript.

DT participated in the initial study design, literature search, collecting data and coordinating the intervention program, tabulated and analyzed the data and drafted the manuscript. LT participated in the literature search, participated and coordinated the data collection and intervention program, assisted the data tabulation and collaborated in writing the manuscript. CPR participated in the initial design of the study, collaborated in the data interpretation and in the critical review of the manuscript at all stages. JAH participated in the initial design of the study, performed laboratory analyzes and collaborated in the critical review of the manuscript at all stages. JDPR participated in the initial study design, performed the laboratory analyzes and collaborated in the critical review of the manuscript at all stages. MSB participated in the initial design of the study, coordinated data collection and the intervention program and carried out a critical review of the manuscript at all stages. All authors approved the final version of the manuscript.

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Resumo

Introdução: Crianças e adolescentes com excesso de peso são mais suscetíveis a apresentarem disfunções metabólicas. No entanto, mudanças no estilo de vida podem prevenir ou retardar o surgimento de fatores de risco, destacando a importância de intervir precocemente nesta população.

Objetivo: Analisar os efeitos de seis meses de um programa de intervenção interdisciplinar sobre os indicadores de resistência à insulina e os níveis de ácido úrico em escolares com sobrepeso e obesidade.

Método: Estudo de intervenção, realizado com adolescentes com excesso de peso, composto por grupo controle (n=19) e grupo intervenção (n=20), que participou de programa de seis meses com intervenção nutricional, psicológica e de exercícios físicos, três vezes por semana. Foi avaliada a circunferência da cintura (CC), realizada coleta sanguínea para avaliação da glicose, insulina e ácido úrico e calculado o índice HOMA-IR, antes e após o programa.

Resultados: O grupo intervenção apresentou redução significativa da circunferência da cintura ($p=0,007$), índice HOMA-IR ($p=0,048$) e ácido úrico ($p=0,036$), após os seis meses do programa; já o grupo controle não apresentou diferenças na pré e pós avaliação.

Conclusão: O programa de intervenção mostrou-se eficiente na redução da circunferência da cintura, HOMA-IR e níveis de ácido úrico em adolescentes com excesso de peso.

Palavras-chave: obesidade, resistência à insulina, ácido úrico, adolescente, estudos de intervenção.

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