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Lifestyle intervention improves lipoprotein particle size and distribution without weight loss in obese Latino adolescents

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Abstract

Childhood obesity is associated with a pro-atherogenic phenotype contributing to increased cardiovascular disease (CVD) risk. This single-arm pilot study examined the effects of a lifestyle intervention on lipoprotein particle size and cholesterol distribution in obese Latino adolescents. Fifteen obese Latino adolescents (15.0 ± 1.0 years) completed a 12-week nutrition education and exercise intervention. Low-density lipoprotein (LDL) particle size and distribution of cholesterol in lipoprotein subclasses were determined via polyacrylamide gel electrophoresis. The intervention resulted in increases in mean LDL particle size (269.3 ± 3.4 to 271.6 ± 2.9 Å, $P = 0.0003$) and cholesterol in large high-density lipoprotein (HDL) subfractions (22.4 ± 11.2 to 26.8 ± 10.6% area, $P = 0.007$) along with decreases of cholesterol in small LDL (1.6 ± 2.0 to 0.6 ± 1.2% area, $P < 0.01$) and HDL subfractions (23.2 ± 9.4 to 19.0 ± 6.7% area, $P = 0.05$). These improvements were observed independent of changes in weight (90.7 ± 26.2 to 89.9 ± 27.8 kg, $P > 0.05$) and suggest that lifestyle modification in obese youth may reduce cardiovascular risk by shifting lipoprotein particle size and cholesterol distribution to a less atherogenic phenotype.

Keywords: Atherosclerosis, cholesterol distribution, LDL size, obesity.

Introduction

Obesity places youth at higher risk for premature morbidity and mortality (1). Obese youth exhibit cardiovascular disease (CVD) risk factors including an atherogenic lipoprotein distribution (2–4) that contributes to atherosclerosis and overt CVD (5). Although the atherosclerotic process begins in childhood (6), traditional markers do not account for the majority of CVD risk observed in adulthood (7). In adults, atherogenic phenotyping that includes classification of size and distribution of LDL-cholesterol (LDL-c) and HDL-cholesterol (HDL-c) predicts incident CVD independent of total LDL-c and HDL-c (8–11). Therefore, including a more comprehensive assessment of lipid markers in youth may improve identification of those at greatest risk for CVD (12).

To date, few pediatric studies incorporate lipoprotein size and distribution measures and whether these markers can be improved in obese youth through lifestyle modification independent of weight loss is not clear. Therefore, the purpose of this study was to determine the effects of a 12-week lifestyle intervention on traditional lipid profiles as well as low-density lipoprotein (LDL) particle size and distribution of cholesterol in LDL-c and HDL-c subfractions in obese youth.

Methods

Fifteen (eight female; seven male) obese (CDC-based body mass index [BMI] percentile = 96.3 ± 4.4) Latino adolescents (15.0 ± 1.0 years) completed a 12-week lifestyle intervention (91% attendance, 3/18 withdrawals), described in detail elsewhere (13). Briefly, weekly nutrition education classes were delivered to adolescents and their families along with 180 min (3 d/week for 60 min) of structured and unstructured physical activities at a target heart rate of 150 beats/min.

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Table 1 Anthropometric measurements, blood pressure, fasting glucose and insulin, and fasting plasma lipids among youth participating in a lifestyle intervention

	Baseline	Range	Post-intervention	Range	*P*
Height (cm)	165.8 (12.1)	151.5–187.6	166.2 (12.2)	151.6–188.5	0.05
Weight (kg)	90.6 (26.2)	57.7–155.0	89.9 (27.8)	55.2–155.7	0.44
Waist circumference (cm)	107.0 (16.7)	84.0–138.7	103.1 (19.5)	76.3–140.5	0.02
BMI (kg m^{-2})	32.5 (6.3)	25.0–47.4	32.0 (6.7)	24.0–46.9	0.08
BMI percentile	96.3 (4.3)	85.9–99.9	95.0 (6.0)	82.2–99.9	0.02
SBP (mmHg)	122 (10)	108–138	118 (9)	100–136	0.03
DBP (mmHg)	71 (9)	51–88	68 (9)	55–89	0.18
Fasting glucose (mg dL^{-1})	89 (8)	76–105	90 (8)	77–110	0.60
Fasting insulin ($\mu U\ L^{-1}$)	19 (10)	7–48	15 (6)	7–29	0.06
TC (mg dL^{-1})	153 (27)	110–197	133 (31)	72–194	<0.001
LDL-c (mg dL^{-1})	90 (24)	55–128	76 (25)	40–131	<0.001
HDL-c (mg dL^{-1})	40 (7)	31–55	39 (7)	23–48	0.61
TG (mg dL^{-1})	141 (55)	58–257	98 (38)	46–159	<0.01

Data are presented as mean (SD).
BMI, body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides.

Table 2 Baseline and post-intervention LDL particle size and cholesterol distribution in lipoprotein subfractions among youth participating in a lifestyle intervention

	Baseline	Range	Post-intervention	Range	*P*
Mean LDL-c particle size (Å)	269.2 (3.4)	262–274	271.6 (2.9)	264–275	<0.001
Large HDL-c (%area)	22.4 (11.2)	10.3–46.2	26.8 (10.6)	13.3–46.4	<0.01
Small HDL-c (%area)	23.2 (9.4)	9.2–36.8	19.0 (6.8)	6.4–27.8	0.05
Large LDL-c (%area)*	25.8 (3.7)	17.8–31.4	24.3 (3.4)	19–31.1	0.11
Small LDL-c (%area)†	1.6 (2.0)	0–6.7	0.6 (1.2)	0–4.6	<0.01

Data presented as means (SD).
*Large LDL-c is a combination of the two largest subfractions.
†Small LDL-c is a combination of the five smallest subfractions.
%area represents % of total cholesterol in each subfraction; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol.

In addition to standard anthropometric measures, fasting (>10 h) serum was collected at baseline and post-intervention (within 24–48 h of last session) to evaluate changes in total cholesterol (TC), LDL-c, HDL-c, triglycerides (TG), and LDL particle size and distribution of cholesterol in LDL and high-density lipoprotein (HDL) subfractions. TC, LDL-c, HDL-c and TG concentrations were determined using an automated analyzer (Cobas c 111; Roche Diagnostics Corporation, Indianapolis, IN, USA). Lipoprotein particles (LDL or HDL) were separated by polyacrylamide tube gel electrophoresis using the Lipoprint system (Quantimetrix Co., Redondo Beach, CA, USA). The amount of cholesterol in each of the bands containing lipoprotein subfractions of different size was quantified by densitometry using the Lipoware software (Quantimetrix Co.) to estimate the proportion of cholesterol in each of the subfractions. Data were analyzed using SPSS 20.0 and are presented as means ± standard deviation. Baseline to post-intervention changes was evaluated by paired sample *t*-test ($P \leq 0.05$). The Arizona State University Institutional Review Board approved the study, and all participants and a parent/guardian provided written informed consent prior to enrolment.

Results

Baseline and post-intervention anthropometric measurements along with fasting serum lipid concentrations are presented in Table 1. Improvements were observed for TC (–20 mg dL^{-1}; 13.1% decrease), LDL-c (–15 mg dL^{-1}; 15.5% decrease) and TG (–43 mg dL^{-1}; 30.5% decrease). Table 2 presents changes in the distribution of cholesterol in different lipoprotein subfractions in response to the intervention. Significant improvements were observed in mean LDL particle size (2.4 Å, 0.9%

increase), the amount of TC in small LDL subfractions (62.5% decrease), and the amount of HDL-c in large HDL subfractions (19.6% increase) and small HDL subfractions (18.1% decrease).

Discussion

This is the first study to demonstrate that lifestyle intervention can improve LDL particle size and distribution of cholesterol in LDL and HDL subfractions independent of weight loss in obese Latino youth. Coupled with changes in traditional lipoprotein measurements, these improvements represent a favourable shift in the atherogenic phenotype and suggest that lifestyle interventions (i.e. changes in dietary patterns and increases in physical activity) can improve early markers of atherosclerosis in youth. Furthermore, weight loss may not be necessary for improvements in these novel markers of cardiovascular health.

Evidence suggests that lipoprotein particle size and the distribution of cholesterol in LDL and HDL subfractions may be better predictors of CVD than traditional lipid profiles (8,9,11,14,15). Because traditional lipoprotein levels were in the normal range at baseline (Table 1), it is possible that improvements in lipoprotein particle size and distribution following diet and exercise may contribute to CVD risk reduction above and beyond levels of and changes in traditional lipoprotein levels (10,11). In adults, the cardioprotective properties of both exercise and diet are related, in part, to favourable shifts in the distribution and size of cholesterol but may be weight loss dependent (16). We did not observe changes in bodyweight and relatively small decreases in BMI percentile and waist circumference. Moreover, neither change in BMI percentile nor waist circumference was correlated with changes in any CVD risk factor (data not shown). Regardless, it is plausible that changes in body composition and/or fat distribution may contribute to the observed improvements independent of weight loss. Alternatively, the observed improvements may be related to the decreases in dietary fat consumption and sedentary time along with increases in cardiorespiratory fitness that were observed (13). These findings have important implications for prevention programs for obese adolescents and are supported by previous work among obese youth showing that improvements in insulin sensitivity following exercise are independent of changes in adiposity (17). It is noteworthy that weight loss in obese youth has also been associated with improvements in cholesterol distribution among lipoprotein subclasses (18). Therefore, obesity-dependent and independent mechanisms underlying improvements in lipoprotein particle size and distribution may be operative.

In children, LDL particle size is associated with traditional markers of CVD risk, including TG and HDL-c (19). In the present investigation, changes in LDL particle size were observed in the absence of changes in total HDL-c (although redistribution of cholesterol in HDL was noted) and unrelated to changes in TG. In support of our data, Azadbakht *et al*. (20) found that reductions in LDL particle size using an NCEP II diet in dyslipidaemic adolescents were unrelated to changes in TG or HDL-c. However, Ferguson *et al*. (21) reported that changes in LDL particle size following exercise in obese pre-pubertal children were correlated with changes in TG. Interestingly, a subsequent study by this same group suggested that changes in both LDL size and TG following exercise training are intensity dependent (22). More work is needed to dissect how intervention parameters such as dietary modification and/or exercise intensity may influence lipid and lipoprotein metabolism in obese youth. In addition, studies should attempt to elucidate the mechanisms underlying the heterogeneity in response to lifestyle intervention as not all youth respond similarly. These studies will help optimize lifestyle intervention delivery within targeted populations.

Our study has several strengths including a translational approach focused on a vulnerable population during a critical developmental period. Despite these strengths, there are limitations that are worthy of comment. The pilot nature of the intervention necessitated a relatively small sample that did not incorporate a control group. However, given the compelling evidence highlighting cardiovascular risk among obese Latino youth (23), the relatively few intervention studies targeting this population, and the ethical considerations for enrolling obese youth into studies that are likely to improve health, we believe our findings extend the available science and represent an important contribution to the current literature. Additional limitations include the relative short duration of the lifestyle intervention, lack of information on pubertal status, and the inability to determine the mechanisms underlying the observed improvements. Furthermore, since this was a comprehensive lifestyle intervention, we were unable to determine the individual impact of and degree to which diet and/or exercise changes influenced lipoprotein profiles. Lastly, although participants did not lose weight, changes in BMI, BMI percentile and waist circumference were observed (13). These changes could reflect significant improvements in body composition

and/or fat distribution that were not assessed. These limitations need to be addressed in future studies.

Conclusion

These findings suggest that lifestyle modification alters the lipoprotein profile in obese Latino youth to a less atherogenic phenotype. Randomized controlled trials that incorporate long-term outcome data are needed to determine the lasting effects of lifestyle intervention on future cardiovascular risk.

Conflict of interest statement

The authors have no conflicts of interest.

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