Original Research Article

A Study of Association Between Serum Paroxanase Enzyme Activity with Dyslipidaemia in Obese Individuals

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Received: 09-09-2021 / Revised: 14-10-2021 / Accepted: 12-11-2021

Abstract

Introduction: Obesity, defined as the excessive accumulation of body fat, is frequently associated with a low concentration, adverse distribution pattern, and abnormal metabolism of HDL particles. Obesity is a highly prevalent chronic state observed in 32% of all adults in the United States. **Material and Methods:** This is prospective study conducted over a period of 6 months among Obese participants were selected at Tertiary care teaching hospital and had never been diagnosed with T2D or prediabetes, as evidenced by an HbA1c of less than 5.5 percent. Healthy volunteers from made up the control group. History of cancer, prior chemotherapy or radiotherapy, diabetes, prediabetes, anaemia, hereditary neuropathies, inborn inconsistencies of metabolism, undiagnosed vitamin/mineral deficiencies, low vitamin B12 or folate tiers that may impact the cornea were all considered exclusion criteria. The Ethics Committee gave their approval to this project. **Results:** We studied 30 participants with severe obesity compared to 30 age-matched healthy controls (P=0.5). The obese group had a significantly higher weight (P<0.0001), waist circumference (P<0.0001) and BMI (P<0.0001), but no statistically significant difference in HbA1c, blood pressure compared to controls. **Conclusion:** Patients with obesity had elevated serum triglycerides and SAA and lower HDL-C, PON-1 activity. Furthermore, obese subjects had higher serum triglycerides and prevalence of metabolic syndrome and lower PON1 activity.

Keywords: Obesity, Cholesterol, Triglycerides, HDL-C.

Introduction

In particular, obesity, defined as the excessive accumulation of body fat, is frequently associated with a low concentration, adverse distribution pattern, and abnormal metabolism of HDL particles[1]. Obesity is a highly prevalent chronic state observed in 32% of all adults in the United States. Moreover, the Framingham Heart Study and the Third National Health and Nutrition Examination Survey have shown a significant increase in lifetime risk of CAD with level of obesity, which may be partly attributed to its association with low HDL-cholesterol levels[2]. Conversely, an increase in HDL-cholesterol levels has been proven to be cardioprotective, such that each 1-mg/dL elevation in HDL reduces CAD risk by 2% to 3%, independently of the levels of low-density lipoprotein and triglycerides[3]. A comprehensive pathophysiological explanation for the association between obesity and increased CAD risk is still lacking. However, because the variation in HDL-cholesterol levels is an important modifiable CAD risk factor in obese states, it is imperative to elucidate the mechanisms which contribute to the lowering of HDL cholesterol in obesity and to determine the efficacy of treatments aimed at raising HDL-cholesterol levels in obese individuals[4].

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The strong inverse relationship between plasma concentrations of high-density lipoprotein (HDL)1 -cholesterol and the risk of developing coronary artery disease (CAD) has stimulated interest in determining the mechanisms and optimal management of low HDL-cholesterol (35 mg/dL)[5]. A number of genetic, lifestyle, and environmental factors have been shown to contribute to the lowering of HDL-cholesterol[6]. Genetic disorders characterized by low HDL-cholesterol concentrations are rare and include mutations in apolipoprotein A-I, the major protein component of HDL, defects in HDL-mediated efflux of cholesterol from peripheral cells through the membrane transporter ABCA1 and hyper catabolism of normal apolipoprotein A-I[7]. In contrast, lifestyle factors— including obesity, physical inactivity, diet, smoking, and advanced alcohol-related liver disease—account for the majority of cases of low HDL-cholesterol levels[8].

This paper will outline the evidence linking obesity to variations in HDL-cholesterol metabolism, characterize the pathophysiologic mechanisms responsible, and examine the efficacy of weight loss achieved with exercise—the recommended non-pharmacologic intervention for increasing HDL-cholesterol levels in obese individuals— on potentially reversing these changes.

Material and Methods

This is prospective study conducted over a period of 6 months among Obese participants were selected at Tertiary care teaching hospital and had never been diagnosed with T2D or prediabetes, as evidenced by an HbA1c of less than 5.5 percent.

Healthy volunteers from made up the control group. History of cancer, prior chemotherapy or radiotherapy, diabetes, prediabetes, anaemia, hereditary neuropathies, inborn inconsistencies of metabolism, undiagnosed vitamin/mineral deficiencies, low vitamin B12 or folate tiers that may impact the cornea were all considered exclusion criteria. The Ethics Committee gave their approval to this project.

Lipid Profile

Total cholesterol was determined by the cholesterol oxidase phenol 4-amino antipyrine peroxidase method, serum triglycerides were determined by the glycerol phosphate oxidase phenol 4-aminoantipyrine peroxidase method, and apolipoprotein A1 was determined by immunoturbidimetric tests. The direct clearing method was used to measure HDL-C. The Friedewald formula was used to calculate LDL.

PON-1 (paraoxonase-1) Behaviour

A moderately micro-titer plate approach employing paraoxon was used to evaluate serum PON-1 activity. A multiclan multiset plate scanner was used to read the plates at 405 nm. CVs were 4% and 4.5 percent intra- assay and inter-assay, respectively.

Statistical analysis

SPSS for Mac was used to conduct the analysis (Version 25.0) The mean and standard deviation are used to express all of the data (SD). The data were checked for normality and statistical analysis were carried out. We employed one-way analysis of variance (ANOVA) or a non-parametric equivalent to analyze differences within and between groups. A significant p value was defined as less than 0.05.

Results

Clinical variables

We studied 30 participants with severe obesity compared to 30 age-matched healthy controls (P=0.5) (Table 1). The obese group had a significantly higher weight (P<0.0001), waist circumference (P<0.0001) and BMI (P<0.0001), but no statistically significant difference in HbA1c, blood pressure or eGFR compared to controls (Table 1). Nineteen (40%) of the participants with obesity fulfilled the criteria for metabolic syndrome.

Table 1: Demographics profile of the obese and control group of participants

Parameters	Control (n = 30)	Obese (n = 30)	P
Demographics			
Age (years)	44.1 ± 7.8	46.9 ± 8.9	0.53
Sex (Female/Male)	17/13	18/11	0.1
Height (cm)	163.0 ± 11.1	164.8 ± 13.1	0.8
Waist circumference (cm)	91.4 ± 11.1	135.1 ± 11.1	< 0.0001
BMI (kg/m^2)	23.1 ± 4.1	48.9 ± 8.4	< 0.0001
HbA1c (%)	4.9 ± 0.8	5.1 ± 0.1	0.64
Systolic BP (mmHg)	128.1 ± 20.1	130.1 ± 18.2	0.5
Diastolic BP (mmHg)	83.2 ± 9.1	81.1 ± 11.3	0.8
Number (%) on statin therapy	0 (0)	1124	< 0.0001
Number (%) with metabolic syndrome	0(0)	1942	< 0.0001

Table 2: Lipid profile of the obese and control group of participants

Lipid Profile	Control (n = 30)	Obese (n = 30)	P
Total Cholesterol (mg/dl)	136.0 ± 6.57	164±3.34	0.03
Serum Triglycerides (mg/dl)	143.0 ± 3.74	220.00±2.75	0.03
HDL-C (mg/dl)	39.66 ±1.78	39.25±2.13	0.51
LDL-C (mg/dl)	67.74±3.72	81±8.83	0.04
VLDL-C (mg/dl)	28.6±1.63	44±2.09	0.03

Table 2. Total Cholesterol, Serum Triglycerides, HDL-C (high density lipoprotein cholesterol), LDL-C (low density lipoprotein cholesterol) are statistical significant difference between two groups.

Lipoproteins and HDL functionality markers

Eleven (23%) of the participants with severe obesity were treated with statins, but their lipid profile, apoA1, apo B and HDL functionality markers did not differ from participants not on statins. Total cholesterol was significantly lower (P = 0.03), but there was no significant difference in HDL-C in participants with severe obesity compared to controls. HDL-C. Serum triglycerides (P = 0.03) were higher and PON-1 activity (P = 0.005) was lower in obese patients. (Table 2).

Table 3: HDL functionality in control and obese participants

Parameters	Control (n = 30)	Obese (-ve) (n = 12)	Obese (+ ve) (n = 18)	*P* value
HDL-C (mg/dl)	39.66 ±1.78	37.23±2.03	38.21±2.05	< 0.0001
apoA1 (mg/dl)	162.1 ± 32.12	143.1 ± 40.12	141.8 ± 22.4	< 0.0001
PON-1 activity (nmol/ml/min)	204.6 ± 99.34	142.1 ± 108.1	51.0 ± 46.99	0.02
SAA (µg/ml)	41.0 ± 38.12	90.1 ± 39.1	84.1 ± 49.14	0.002
Cholesterol efflux (%)	17.9 ± 5.60	14.6 ± 3.70	16.1 ± 4.10	0.002

Table 3. HDL functionality in control and obese participants. Results reported as mean ± standard deviation. HDL-C, high density lipoprotein cholesterol; apoA1, apolipoprotein A1; PON-1, paraoxonase-1; SAA, serum amyloid A.

Discussion

The increasing prevalence of obesity in the last decades has become a major health problem worldwide. The number of overweight and obese people is ever increasing and is becoming more common in children and adolescents. The causes of obesity are multifactorial, with the most important factors being excess calorie intake and lack of physical activity[11]. Excessive body weight increases the risk of disease development, such as coronary artery disease, hypertension, type-2 diabetes mellitus, and dyslipidaemia. High levels of triglyceride-rich lipoproteins and low levels of high-density lipoprotein cholesterol (HDL-C) commonly characterize dyslipidaemia in obesity[9].

In obesity, not only HDL levels are altered, but an altered HDL distribution pattern and abnormal HDL metabolism have also been observed, which often leads to dysfunction of the HDL particles[10]. Consequently, the focus has shifted from studying the quantity of HDL to studying the quality of HDL[11]. Further, also focus on obesity-induced changes in HDL composition and the concomitant changes of HDL functionality[12,13]. Another aspect will be the relationship of HDL with the adipokine adiponectin as well as with the bioactive lipid sphingosine-1-phosphate (S1P), whose levels are altered in the state of obesity. They also summarize the effects of weight loss induced by bariatric surgery, Mediterranean diet and pharmacological approaches, which effectively increase HDL-C levels and improve HDL function[14,15].

The biogenesis of HDL starts in the liver and the intestine, where apolipoprotein (apo) A-I is synthesized. After secretion, lipid-poor apoA-I interacts with the integral cell membrane protein ATP-binding cassette transporter A1 (ABCA1), which is abundantly expressed by hepatocytes and enterocytes[16]. Through interaction, apoA-I acquires lipids from the cellular lipid pool, generating nascent HDL particles. Additional lipids and apolipoproteins are acquired, which are derived from hydrolysis of triglyceride-rich lipoproteins[17]. This process partly explains the strong inverse relationship of HDL-C and triglyceride levels, often observed in obese subjects[18].

The acquired cholesterol of HDL is further esterified by lecithin-cholesterol-acyl transferase (LCAT), forming mature HDL particles. The reaction takes place at the surface of HDL and requires apoA-I as an activator for LCAT[19]. The generated HDL-associated cholesteryl-esters are partially transferred to apoB-containing lipoproteins by cholesteryl-ester transfer protein (CETP), usually in exchange for triglycerides. Another pathway for clearance of cholesteryl-ester in HDL is the direct uptake by the liver via scavenger receptor class B type 1 (SR-BI). After interaction of SR-BI with large cholesterol-rich HDL, cholesteryl-esters and free cholesterol are internalized and cholesterol is removed through the bile, while apoA-I dissociates[20].

Conclusion

In conclusion we show there is evidence of Patients with obesity had elevated serum triglycerides and SAA and lower HDL-C, PON-1 activity and cholesterol efflux. Furthermore, obese subjects had higher serum triglycerides and prevalence of metabolic syndrome and lower PON1 activity.

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Conflict of Interest: Nil Source of support: Nil

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