**Effect Of Aerobic Exercise And Diet On Lipoprotein-Associated Phospholipase A2 In Obese Egyptian Patients**

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**Abstract:** Lipoprotein-associated phospholipase A2 (Lp-PLA2) is a novel inflammatory biomarker that is associated with increased cardiovascular disease risk independent of and additive to traditional risk factors. Lp-PLA2 activity is correlated with the degree of inflammation in the atherosclerotic plaque and is associated with low-density lipoproteins (LDL). **Objective:** In this present study, we examined the efficacy of combination of aerobic physical activity and diet control without hypocholesterolemic drugs on reducing the Lp-PLA2 levels. **Methods:** This prospective study includes 30 hypercholesterolemic obese Egyptian patients (50% men and 50% women) who completed the aerobic physical activity and diet control for 3 months. Initial and after protocol complete the following were assessed: weight, body mass index (BMI), Lipid profile and the Lp-PLA2 levels. **Results:** The study revealed a 6.21% reduction in mean Lp-PLA2 values (baseline 24.63 ± 2.74 vs 23.1±2.65 ug/L after protocol complete; P < 0.001). The change observed in low density lipoprotein (LDL-C) was 17.46 %, (baseline 174.36± 38.5 vs 143.9±32.33mg/dL after protocol complete), which also was significant (P < 0.001) and high density lipoprotein (HDL-C) was 15.83 %, (baseline 31.96± 4.57vs 37.03±4.45 mg/dL after protocol complete), which also was significant (P < 0.001). **Conclusion:** Lp-PLA2 is reduced with the use of combined aerobic physical activity and diet control without lipid lowering therapy. This change in Lp-PLA2 may be partially explained by the changes in LDL-C.

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**1. Introduction**

Despite considerable progress in atherosclerosis prevention (primary or secondary) by treating its risk factors, a residual risk responsible for cardiovascular (CV) diseases mortality and morbidity worldwide persist1**.** Several approaches aimed to identify asymptomatic individuals who will benefit from these preventive therapies.

Obesity is an independent risk factor for CV diseases and Inflammation has been established as a major mechanism of all stages of atherogenesis and linked it to other features of the metabolic syndrome (hypertension, dyslipidemia and type 2 DM as well as many other conditions). Inflammatory biomarkers have been linked to the epidemiology of CV risks and the identification of a novel target previously unrecognized could help prevention2**.**

Lipoprotein-associated phospholipase A2 (Lp-PLA2) is a novel CV biomarker. Lp-PLA2, also known as platelet-activating factor acetyl hydrolase, is a 50-kD Ca-independent phospholipase that is distinct from another macrophage product. Lp-PLA2 is the only enzyme responsible for the hydrolysis of oxidized phospholipid resulting in the production proinflammatory and cytotoxic products (lysophosphatidylcholine and oxidized fatty acid)3. It is relatively unique due to its high specificity for vascular as opposed to systemic inflammation and approved by the Food and Drug Administration as a predictor of cardiovascular risk. Lp-PLA2 is known to be a good predictor of both first-ever coronary events and ischemic stroke in population-based studies4. Experimental studies suggest its role in the formation of advanced rupture-prone atherosclerotic lesions5**.**

Physical activity is the most variable component of energy expenditure and is an important component on long-term weight control and hypercholesterolemia6. Exercise as an anti-cholesterol treatment does not work for everyone7.

Diet containing low saturated fats, plant sterols and plenty of soluble fiber decrease LDL and may also HDL. Keeping HDLs high is important because it is estimated that for every 1 mg/dl increase in HDL, the risk for coronary heart disease is reduced by up to 3 percent8.

Doing aerobic exercise along with diet changes can prevent or decrease a drop in HDLs but uncertain about their effect on lipoprotein-associated phospholipase A2 especially in obese hypercholesterolemic patients so this study aimed to assess this effect.

**2. Subjects and Methods**

This study included thirty obese patient with body mass index > 30 Kg/m2 and total cholesterol level > 200 mg/dl from those attending the outpatient clinic of the Kalup ELaam Hospital and a private clinic in the period between March 2011 and February 2012.

**Inclusion criteria:**

Both genders aged between 30 and 45years, obese patients (more than 30 Kg/m2) with elevated lipid profile (total cholesterol level > 200 mg/dl) and had sufficient cognition and education to understand the requirements of the study.

**Exclusion criteria:**

The exclusion criteria were smoking, hypertensive patients, known ischemic patients, diabetic patients, Refusal of patients to be enrolled in the study, the use of lipid-lowering drugs and anti-inflammatory drugs, the presence of any acute disease, contraindication to exercise and pregnancy or breastfeeding.

All patients subjected to

1-Informed consent after explanation of the study protocol.

2-Weight and height measurement in all participants and calculation of BMI from the formula:

BMI= weight (kg)/ height (m2)9.

2-Serum analysis for lipid profile after 10-14 hours fasting using (Model; Bio system photometer, wave lenght; 546mm Made in Spain) for measuring HDL-C, triglyceride and total cholesterol level and LDL-C was calculated using the Friedewald equation

LDL-C as (total cholesterol) = (high-density lipoprotein cholesterol [HDL-C]) − (triglycerides / 5) in mg/dL10, at the initial start and after 12 weeks of diet and exercise protocol.

3-Human lipoprotein-associated phospholipase A2 at the initial start and after 12 weeks of diet and exercise protocol. Lp-PLA2 s measurement was determined by a Food and Drug Administration-cleared ELISA assay (PLAC test, diaDexus, Inc., South San Francisco, CA). The PLAC test is based on the principle of a sandwich enzyme immunoassay that uses two specific IgG monoclonal antibodies (2C10 and 4B4) described by **Caslake11**.

4--Healthy diet recommendations that is low in saturated fats, high plant sterols and soluble fibers (more in vegetables and fruits) for 12 weeks.

5- Aerobic exercise in the form of walking more than 40 minutes 5 times /week. The duration of exercise divided into (warm up; 5minutes, active phase; 20-30 minutes and cool down; 5minutes) for 12 weeks.

6- Follow up for 12 weeks with re-assessment of BMI, lipid profile and lipoprotein-associated phospholipase A2 levels

7- Data collection and statistical analysis:

The data was collected before and after treatment program. The data collection sheet was analyzed statistically by using paired t test. The mean value and standard deviation of each group was calculated for each variable pre and post treatment using SPSS 17 (SPSS, Inc, Chicago, IL).

**3. Results**

**A-Basline characteristics of the Subjects:**

1. **Demographic characteristics:**

The demographic data of the studied population in table (1) age (37.33±5.36) years, gender (15 males and 15 females weight (108.23±14.69) kilograms (Kg), and BMI (44.06±6.61) (Kg/m2).

Table (1): Characteristics of patients.

|  |  |
| --- | --- |
| **Items (30 patients)** | **Mean±SD** |
| **Age (yrs)** | 37.33±5.36 |
| **Male gender** | 15 (50%) |
| **Weight (Kg)** | 108.23±14.69 |
| **BMI (Kg/m2)** | 44.06±6.61 |

SD: standard deviation

1. **Laboratory finding at initial study**

The laboratory finding of the studied population demonstrated in table (2).

Table (2): Laboratory results of patients.

|  |  |
| --- | --- |
| **Items (30 patients)** | **Mean±SD** |
| **Total Cholesterol (mg/dL)** | 231.63±37.43 |
| **S.triglycerides (mg/dL)** | 150.33±25.08 |
| **LDL(mg/dL)** | 174.36±38.5 |
| **HDL (mg/dL)** | 31.96±4.57 |
| **Phospholipase A2 (ug/L)** | 24.63±2.74 |

\*SD: standard deviation, P: probability

**B-Follow up results:**

**1-Body weight:**

Table (3) demonstrated the Body weight pre and post treatment. There was a significant difference in the paired t-test between pre and post the protocol where the body weight were reduced from 108.23± 14.69 kg to (94.4±10.03 kg) and P-value was (0.0001).

**2-BMI:**

There was a significant decrease in BMI between pre and post the from 44.06± 6.61to 38.43±6.33 kg/m2) where P-value was (0.0001), table (3).

**3-Lipid profile:**

There was a significant decrease in total cholesterol as shown in table (4) and figure (1) between pre and post protocol (from 231.63± 37.43 to 203.4±30.91), triglyceride ( from150.33± 25.08 to136.66±21.4) and LDL (from 174.36± 38.5 to 143.9±32.33) while increase of HDL (from 31.96± 4.57 to 37.03±4.45) and P-value was (0.0001).

Table (3): Body weight and BMI pre and post the protocol.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Item** | **Mean±SD** | **% of improvement** | **t-value** | **P-value** |
| **Body weight** (Kg**)** | **Pre** | **108.23±14.69** | **12.77 %** | **20.24** | **0.0001** |
| **Post** | **94.4±10.03** |
| **BMI** (Kg/m2) | **Pre** | **44.06±6.61** | **12.77 %** | **20.0** | **0.0001** |
| **Post** | **38.43±6.33** |

SD: standard deviation, P: probability

Table (4): Lipid profile pre and post the protocol.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Item** | **Mean±SD** | **% of** **improvement** | **t-value** | **P-value** |
| **Total Cholesterol** (mg/dL) | **Pre** | 231.63± 37.43 | 12.18 | 7.53 | 0.0001 |
| **Post** | 203.4±30.91 |
| **S.triglycerides** (mg/dL) | **Pre** | 150.33± 25.08 | 9.08 | 9.31 | 0.0001 |
| **Post** | 136.66±21.4 |
| **LDL**(mg/dL) | **Pre** | 174.36± 38.5 | 17.46 | 5.5 | 0.0001 |
| **Post** | 143.9±32.33 |
| **HDL**(mg/dL) | **Pre** | 31.96± 4.57 | 15.83 | 10.96 | 0.0001 |
| **Post** | 37.03±4.45 |

SD: standard deviation, P: probability

Table (5):phospholipase A2 level pre and post the protocol.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Item** | **Mean±SD** | **% of improvement** | **t-value** | **P-value** |
| P**hospholipase A2** (ug/L) | **Pre** | 24.63± 2.74 | **6.21** | **10.25** | **0.0001** |
| **Post** | 23.1±2.65 |

SD: standard deviation, P: probability

**4-Phospholipase A2:**

There was a statistically significant decrease difference in Phospholipase A2 between pre and post the protocol (from 24.63± 2.74 to 23.1±2.65) with P-value (0.0001), table (5) and figure (2).

Fig.(1): Lipid profile pre- and post- treatment**.**

Fig.(2): Phospholipase A2 level pre- and post- treatment**.**

Fig.(3): Number of cases with LDL > and <130 mg/dl pre- and post- treatment**.**

The data in Fig.(3) represented the number of patients with LDL more and less than 130 mg/dl pre and post treatment. Pre treatment the number of cases with LDL less than 130 mg/dl was 5 (16.67%) and the numbers of cases with LDL more than 130 mg/dl was 25 (83.33%). Post treatment the number of cases with LDL less than 130 mg/dl was 11 (36.67%) and the numbers of cases with LDL more than 130 mg/dl was 19 (63.33%).

**4. Discussion**

Coronary artery disease is the leading cause of morbidity and mortality worldwide. The identification of patients at risk for coronary events and those in the early stages of atherosclerosis is essential for primary and secondary prevention. Coronary endothelial dysfunction can be considered a marker for early atherosclerosis12and has been shown to be associated with an increased risk of ischemic cardiac events and stroke13.

Metabolic syndrome is a group of risk factors that raises the risk for heart disease and other health problems, such as diabetes and stroke14.

Lp-PLA2 is an enzyme that degrades oxidatively fragmented phospholipids, which may play a major role in atherogenesis12. Plasma Lp-PLA2 activity is primarily associated with LDL, while a small proportion of the enzyme activity is associated with HDL. Epidemiological studies reported that increased Lp-PLA2 mass or activity was associated with an increased risk of cardiac death, myocardial infarction, acute coronary syndromes and ischemic stroke15. Reduced LP-PLA2 could have anti-inflammatory actions, improve endothelial function, reduce platelet aggregations, and has a favorable affect on autonomic tone

There has been limited research examining the association between Lp-PLA2 and physical activity. However, we found no reports of studies demonstrating the effects of low saturated fats, high plant sterols and soluble fibers (more in vegetables and fruits) diets on Lp-PLA2 concentration. In spite of this, considering that such dietary regimens reduce LDL-C particles as well as overall vascular inflammation, the dietary changes in this study may have played a possible role in lowering Lp-PLA2 mass concentration16.

In this study 30 obese hypercholesterolemic after three months continuous aerobic exercise and diet control have been studied. Extracted result after 3 months training showed that regular aerobic exercise and diet control can make significant changes in concentration of blood serum lipids including cholesterol, triglyceride, LDL, HDL and lipoprotein associated phospholipase A 2.

The BMI (obesity index) significantly decreased after aerobic exercise. Since the total body weight decreased by 12.77%, the weight loss is attributed to a decrease in fat. The concentration of HDL-C significantly increased by 15.83%. A significant reduction in serum triglyceride concentration was observed (9.08%). However, the total cholesterol in serum was altered by 12.18%,low density lipoproien (LDL-C) reduced by 17.46% and little change in phospholipase A2(PL-LPA2) by 6.21%.

Therefore, the negative association detected between combined aerobic exercise and diet control and Lp-PLA2 in obese hypercholesterolemic patients would suggest a way of blocking the sequence of events leading to plaque formation and rupture present later in their life.

This research as regard aerobic exercise and lipid profile is consistent with **Kraus et al. 17,** as the regular aerobic exercise decreased the mean of cholesterol concentration. (**Jakicic et al.18,** who found that combination of physical activity with modifications to energy intake had the most effective behavioral approach for addressing the obesity epidemic. **Grandapur19** and his collogue` findings. They proved that regular aerobic aerobic exercise is the cause of decrease in concentration of cholesterol, triglyceride and LDL.

The results of this study agree with Kodama20 who demonstrated that: aerobic exercise affect HDL: participants had increases in HDL cholesterol averaging about 2.5 mg/dL. This increase in HDL cholesterol was only modest, but was statistically significant.

In 2010 **Reddy et al. 21,** studied the effect of life style and statin, fenofibrate, niacin and omega3 effect on LP-PLA2 and found reduction of 32% but they not study diet and exercise alone.

In a small interventional study that assessed the effect of a low-calorie diet on Lp-PLA2 activity levels, **Tzotzas et al.22** found that an average 10-kg weight loss achieved over 4 months was associated with a 10% decrease in Lp-PLA2 activity. All participants received the same low-calorie diet and, thus, the effect of specific nutrients on Lp-PLA2 activity could not be distinguished from the effect of weight loss on Lp-PLA2 activity. However, this evidence in conjunction with exercise observed in our study suggested that diet may represent a potentially modifiable pathway through which Lp-PLA2 activity can be altered.

In the present study, being overweight; it is possible that the relation between BMI and Lp-PLA2 is mediated entirely through the lipid pathways, but this relation is likely more complex and warrants further study.

The influence of the nutritional status on LpPLA2 activity was also evaluated in adolescents where it was positively associated with body mass index, waist circumference and fat mass percentage 23**.** Finally, **Chen et al. 24** compared vegetarians with omnivores and observed that vegetarians presented lower Lp-PLA2 activity, with lower total cholesterol and LDL-cholesterol, but with increased chances of higher C-reactive protein.

**5. Conclusion**

In conclusion, short-term supervised aerobic exercise program with diet control in obese patients is beneficial and resulted in significant weight reduction with concomitant improvement of lipid profile and phospholipase A2 level.

**6. Limitations**

The present study, however, is limited by its small sample size, and lack of control group. Also, in this study we didn’t results on baseline versus post-treatment calorie intake, dietary composition, and quantitative measures of energy expenditure during exercise.

**7. Recommendations**

The findings of the current study recommends that:

1. Lipid profile improvement should be considered when designing rehabilitation program of hyperlipidemia.
2. In management of patients of hyperlipidemia, attention to aerobic exercise, diet and lifestyle modification.
3. Replicate the same study on a large sample number and different age groups.
4. Study the effect of adding anti-hyperlipidemic drugs on phospholipase A2 level.
5. Assess the effect of aerobic exercise on lipid profile after long controlled review of 1 year

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