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**Editorial**

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# Plasma Apo-M Response to a Circuit Resistance Training Program

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## INTRODUCTION

High-density lipoprotein (HDL) cholesterol has been recognized as a key variable in prevention of arthrosclerosis and some cardiovascular diseases related to its low / very low levels in blood circulation. Considering HDL compositions and actions, it is well-known that HDL, via its elements, acts as an anti-inflammatory action in endothelium and leukocytes, endothelial cell proliferation and migration, regulation of VSM cells, regulation of platelets, modulation of glucose homeostasis, modulation of adipose, signaling, anti-oxidative, and anti-atherogenic (1-4). Apoproteins or apolipoproteins are key elements and responsible for triglycerides and cholesterol transports through the blood circulation to other tissues or organs. In this regard, HDL plays a crucial role in cholesterol return back from tissues to the liver for more degradation and excretion. Considering the apolipoproteins, it has been suggested that the term of apo-proteins or apolipoproteins is an extension of that used to describe the protein of enzymes with cofactors, the apo-enzymes, and thus any protein associated with lipids or a lipoprotein particle can be considered as an apolipoprotein that is part of a holo-particle, but this word is mostly used for the classical apolipoproteins such as apoAI, apoAII, apoB100, apoC, apoD, apoE, and apoF (5). However, according to Davidsson *et al.* (2010) who suggested that other plasma proteins, including enzymes and lipid-transport proteins, can exist in association with lipoproteins and are in equilibrium with non–lipoprotein associated forms which could be used as the term "associated proteins" for these plasma proteins that remain bound to lipoproteins after their isolation (5). The apolipoprotein constituents of the major plasma lipoproteins which regulate lipoprotein metabolism and determine the unique role of these lipoproteins in cholesterol transport and lipid metabolism (5, 6). In addition to the above-mentioned apolipoproteins, other classes of apolipoproteins such as; apoG, apoH, apoJ, apoL, apoM, apoN, and apoO have also been reported by several researchers (6-10). It has been suggested that HDL posses different types of apolipoproteins such as apo A, particularly apoA-I which is generally representing about 70%-80% of HDL protein by weight and apo-A-II about 20%. In addition to apoA-I and apo-II, other proteins such as apoA-IV, apoA-V, apo C-I, C-II, a C-III, apoD, apoE, apoF, apoH, and ApoJ, apoM , apoN, and apoO exist in HDL at very small amounts (6, 8, 9, 11, 12). Apolipoprotein M (Apo-M) is a novel human protein of apolipoprotein classes with 188 amino acids that are identified, characterized and highly expressed in liver and kidney tissues. ApoM is mainly associated with high-density lipoprotein (HDL), and acts as a chaperone for sphingosine-

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1-phosphate (S1P), promotes mobilization of cellular cholesterol and a new biomarker in sepsis. The level of apoM in plasma/serum is affected by several factors such as pregnancy, hyperglycemia, plasma leptin concentration, obesity, diabetes, insulin concentration (5-13). The effects of different types of regular aerobic exercises and somewhat an endurance type of resistance training on plasma lipids, lipoproteins, particularly on high density-lipoprotein (HDL) and its compositions have been well-documented. However, the effect of circuit resistance training (CRT) with or without milk products administration on a novel-introduced apolipoprotein M (ApoM) has not been studied yet. This study was conducted to investigate the effect of 4 weeks of CRT program in untrained high school students.

## MATERIALS AND METHODS

The study was approved of by the Ethics Committee of the Sciences of the University of Mazandaran (UMZ) and Babol University of Medical Sciences (BUMS) in Mazandaran, Iran with the policy statement of the Declaration of the Iranian Ministry of health.

**Subjects.** The Written consent was obtained from the 12 young male and untrained high-school students (age 17.25±0.44 y, height 176.57±1.45 cm, body weight 70.8 ± 6.5, and body mass index (BMI) 20.19 ± 1.70kg/m2) without weight circuit-resistance training experiences were employed and randomly assigned to two groups; Training-Water (TW, n=7), Training-Milk (TM, n=7). Subjects received either tap water (400 cc) or low fat milk (400cc), immediately after training sessions. It should be noted that the solution has been administrated gradually.

**Training protocol, plasma apolipoprotein-M, and Statistical analysis.** The circuit resistance training was performed according to Ghanbari-Niaki (2006) (14) and Ghanbari-Niaki *et al.* (2007) (13) with a modest modification in the number of exercises (bench press-off pins, inclining bench press, cable push-down, deadlift halter, squat 90° over neck, back extension on roman chair, crunch with free weight, leg press, leg extension, seated calf raise). Subjects were asked to perform circuit resistance training for 45-50 minutes/session, 3 days/week and for 4 weeks. Each training session consisted of warm-up (10min), cool-down (10min), and circuit resistance of 10 exercises (25 seconds for each exercise, 8-12 repeats, 2 rounds/session with 5 minutes rest period between rounds) to strengthen most of the large muscle groups. Each load corresponded to 60% of the individual one-repetition maximum. All exercises were conducted with the use of free weight and machine. The subjects were instructed to follow a normal lifestyle to maintain daily habits, to avoid any medications, and to refrain from exercise 3 days before the blood sampling. Blood samples were obtained from an antecubital vein 72 hours before and 72 hours after the last circuit resistance training session while the subjects fasted overnight (at least 12h). Plasma samples were immediately frozen and stored at −20°C and −80°C for subsequent analyses (within 4-6 weeks). Plasma Apo-M was determined by using a commercial human Apo-M, ELISA Kit (Catalog Number-CSB-EL001947HU, CUSABIO-BIOTECH, China) with detection range 1.56 ng/ml-100ng/ml, sensitivity 0.39 ng/ml, Intra-assay precision : CV% <8%, and Inter-assay precision: CV%<10%. After normalization of data by suitable test, dependent and independent *t*-tests were employed. All the data were reported as mean ± SE. A significant difference was accepted at alpha P ≤05. All statistical analyses were performed with SPSS (Version 13; SPSS, Chicago, IL).

## RESULTS, DISCUSSION, and CONCLUSION

Data analysis showed that plasma ApoM concentrations were reduced at the end of training programs in both TW and TM groups, but a significant (P<0.004) reduction in plasma ApoM concentration was observed in TM group. There was no significant difference between TW and TM groups (Fig.1).

The main findings of this small, but important and new study were reduction of plasma ApoM levels after training and the ability of employed kit to detect ApoM in obtained plasma samples. This detection of plasma ApoM in our experimental condition is in agreement with

other studies, but considering the ApoM level itself, there is a disagreement with the present result with those reported by Xu and Dahlback (1999), Christoffersen *et al.* (2006) and Axler *et al.* (2007), Memon *et al.* (2013) (10, 15-17).

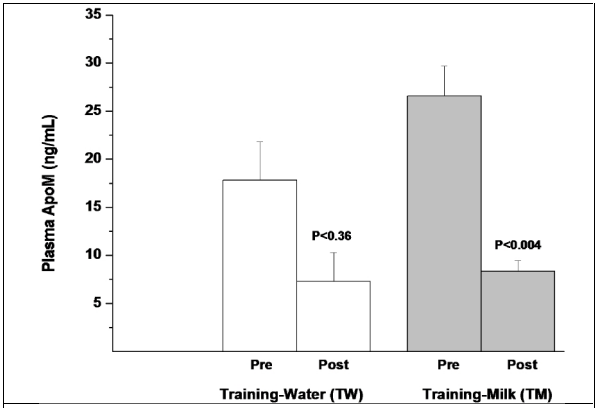


Figure 1. Plasma Apo-M Response to a Circuit Resistance Training Program

In the study by Cervin *et al.* (2010) (18) who used an ELISA kit [Axler *et al.* 2007 kit (15)] for serum ApoM determination, the value for ApoM was ranged from 0.7 to 1.16 µmol/L. In the discussion of this study, Cervin *et al.* (18) also mentioned a controversial reported result. They suggested that one obvious difference is the estimated mean normal concentration of apoM in plasma for the diabetes type 2 control individuals in the three studies. The levels in this study (24 mg L) (2) and by Skupien *et al.* (14 mg L) (2) are substantially lower than that found by Richter *et al.* (100 mg L) (2). This may possibly reflect differences in specificity of the antibodies in the respective assays to the standard, which in the ELISA is a human normal plasma pool and, in the blot-based assays, recombinantly expressed apoM. The levels of plasma is no direct evidence/information or study about the effect of physical exercise training, particularly circuit resistance training and milk supplementation on plasma ApoM. This is the first and direct report about the alteration of plasma ApoM response to circuit resistance training. However, in a comprehensive study, Axler *et al.* (2007) (15) reported that the ApoM content in the healthy human plasma pool was 0.94 mM, or ~23 mg/l. This roughly corresponds to $1/50^{th}$ of the mean molar concentration of apoA-I in plasma. They also suggested that in answer to this question that whether strenuous sporting activity in the week before sampling affected ApoM concentration was investigated with students' T-test. The group that had performed strenuous exercise (mean concentration, 0.87 mmol/l; n 5 71) showed a statistically significantly lower mean ApoM concentration compared with the non-exercise group (mean concentration, 0.93 mmol/l; n 5 524, P 5 0.019). However, the exercise group also had a significantly lower mean plasma cholesterol level (4.8 vs. 5.5 mmol/l; P, 0.001), and in a multiple-regression analysis of ApoM concentration, with cholesterol as the other independent variable, exercise did not contribute significantly to the mode. The mechanisms by which a circuit resistance training program (4weeks) was able to decrease plasma ApoM levels in high school students are not known. However, it has been suggested that ApoM is highly expressed in the liver and, kidney and very low (less than 5%) in human, another mammalian tissues (19). In the liver, apoM is expressed in hepatocytes and mainly secreted into the plasma, where it becomes integrated in plasma lipoproteins. Most of the human apoM in the blood is a component of HDL, but it is also found in other lipoprotein classes (19). A reduction in plasma ApoA at the end of circuit resistance training might be due to a decrease in ApoM expression in liver, a reduction in ApoA-1, an training-induced diabetic-like situation or by an increase in ApoM urinary excretion (19-21). In summary, the present result indicates that the used kit was able to detect ApoM in high school student plasma samples. The results also showed that ApoM levels were dramatically decreased at the end of circuit resistance training program. This stud also opened a new avenue for future research in relation to the impact of different types of physical exercise on HDL-ApoM and effective factors on it. Further investigations by using different methods and different kits are warranted.

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