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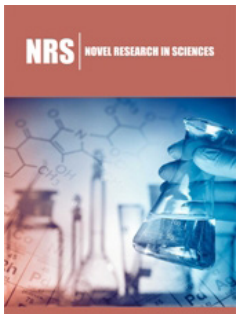
Mini Review

Effects of Sibutramine Treatment on Serum Lipoproteins and Il-6 Levels in Rats Fed with High Protein Diet



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Abstract

The aim of the study was to explore the effects of macronutrients and Sibutramine(S) on serum IL-6 and lipoprotein levels in rats fed with standard laboratory diet (SD) and High protein diet (HPD). Two groups of 21 male Wistar rats consumed SD or HPD for 13 weeks. In the last 3 weeks each of them was divided into 3 subgroups received vehicle, Sibutramine 5 or 10mg/kg. Serum lipoproteins and IL-6 were assayed. Serum HDL-CHOL was lower in the SDS0 compared to HPDS0group, in the SDS5 compared to HPDS5, in HPDS10 compared to HPDS5. Sibutramine administration did not affect serum IL - 6, HDL or LDL in any diet group at any dose.

Keywords: IL-6; Sibutramine; High-protein diet

Abbreviations: SD: Standard laboratory Diet; HPD: High Protein Diet; S: Sibutramine;

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Introduction

IL-6 is a pleiotropic cytokine that plays an important role in host defense by regulating immune and inflammatory responses. Produced by T cells, monocytes, fibroblasts, endothelial cells and keratinocytes, IL-6 has diverse biological functions. It stimulates B-cell differentiation and antibody production, synergizes with IL-3 in megakaryocyte development and platelet production, induces expression of hepatic acute-phase proteins, and regulates bone metabolism [1]. IL-6 is a mediator of inflammatory and immune responses, which also affects a variety of metabolic processes as an autocrine and paracrine regulator of adipocyte function [2,3]. Sibutramine is a nor adrenaline and serotonin reuptake inhibitor, that induces weight loss by increasing energy expenditure and decreasing caloric intake. Moreover, it ameliorates insulin resistance and has beneficial effects on serum lipoproteins [4,5]. The aim of the study was to explore the effects of macronutrients and sibutramine on serum lipoproteins and plasma IL-6 levels in rats fed with standard or High protein diet.

Material and Methods

42 male Wistar rats 2 months old, weighting 180±10g were acclimated to constant environmental conditions: 12/12-hour light/dark cycle, 24 °C room temperature, and 45% humidity. After acclimation the rats were separated in 2 Groups according to diet given for 13 weeks. Rats of each group were individually caged and fed ad libitum with Standard chow Diet (SD)(n=21), or with High Protein Diet (HPD)(casein 64%) (n=21). From week 10th to 13th rats of each groups were divided into 3 subgroups (n=7/subgroup) and received single daily i.p. injections of: vehicle (saline-subgroups SDS0, HPDS0), sibutramine-HCL(S) 5mg/kg (subgroups SDS5, HPDS5) and S 10mg/kg (subgroups SDS10, HPDS10). At the end of the study, rats were euthanized under light anesthesia with a mixture of ketamine and xylazine HCL (i.m. injection of 1:0,1mg/kg). Blood was collected right before death, from vena cava inferior and serum was separated and stored at -70 °C for subsequent measurement of IL-6

concentration by enzyme-linked-immunosorbent assay. The Mouse IL-6 solid-phase sandwich ELISA (enzyme-linked immunosorbent assay) is designed to measure the amount of the target bound between a matched antibody pair.

A target-specific antibody has been pre-coated in the wells of the supplied microplate. Samples, standards, or controls are then added into these wells and bind to the immobilized (capture) antibody. The sandwich is formed by the addition of the second (detector) antibody, a substrate solution is added that reacts with the enzyme-antibody-target complex to produce measurable signal. The intensity of this signal is directly proportional to the concentration of target present in the original specimen. Moreover, concentration of Lipids [HDL cholesterol (HDL-CHOL), LDL cholesterol (LDL-CHOL) and Triglycerides] in serum was calculated by autoanalyzer. Significant differences between groups and subgroups were determined by one-way analysis of variance (ANOVA). Statistical significance was set at 0.05.

Results

Lipids levels

Serum LDL-CHOL concentration was not statistically different between the subgroups of SD (p=0.084 and of HPD(p=0.238). Serum HDL-CHOL was lower in the SDS0 compared to HPDS0(p=0.03) group, in the SDS5 compared to HPDS5(p<0.001), in HPDS10 compared to HPDS5(p=0.013). Serum HDL-CHOL was not statistically different between the subgroups of SD (p=0.174). Serum triglycerides were not statistically different between the subgroups of the SD(p=0.207) and HPD(p=0.426) (Figure 1).

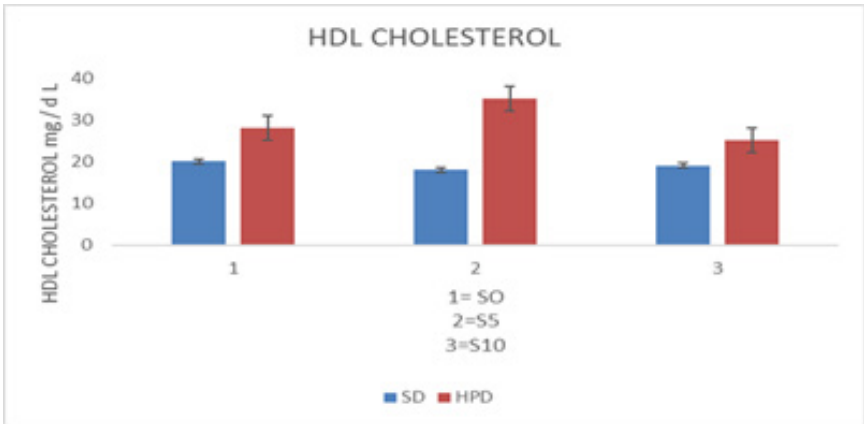

Figure 1: Serum HDL cholesterol levels of rats fed the SD or HPD after vehicle or sibutramine treatment.

IL-6 Concentration

Serum IL-6 concentration was not statistically different between the subgroups of SD (p=0.585) and HPD(p=0.468) (Figures 2 & 3). Diets rich in protein have been associated with good effects on serum triglycerides, probably due to the low proportion of carbohydrates. The administration of SD diet was associated with a favorable LDL cholesterol profile. It is possible that the adherence to a diet that offers all macronutrients prevents both excessive free fatty acid synthesis observed in diets with a low fat/carbohydrate ratio, as well as adiposity and hyperphagia [6]. However, the beneficial effect of the standard diet was restricted by its effect of serum HDL cholesterol. Sibutramine did not affect IL -6 at any dose. This is the first experimental study evaluating the effect of sibutramine on IL -6 levels. Further studies will be needed to demonstrate the long-term effects of sibutramine administration on IL-6 levels.

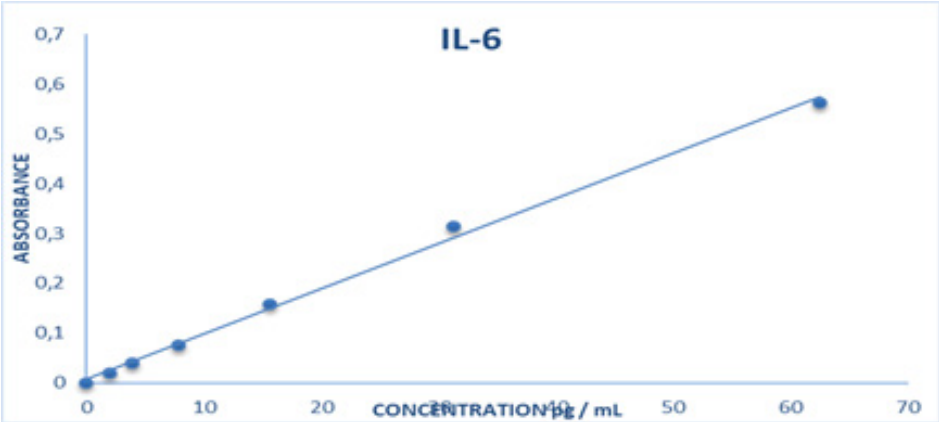

Figure 2: IL-6 standard reference curve.

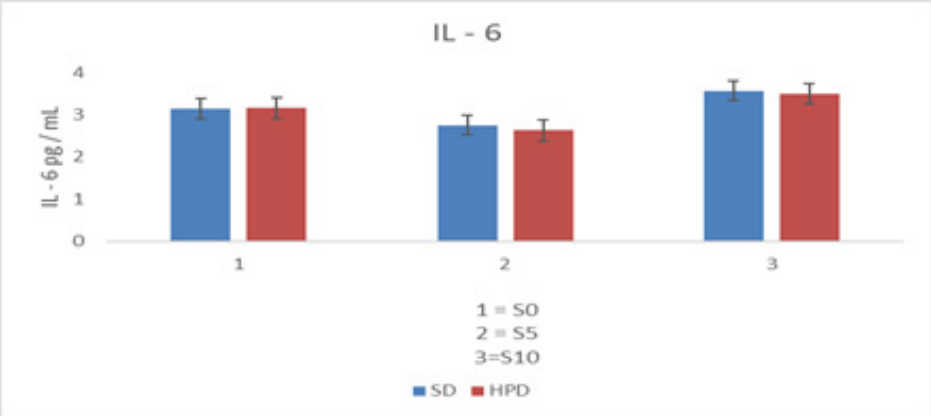

Figure 3: Serum IL-6 levels of rats fed the SD or HPD after vehicle or sibutramine treatment.

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