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Original Research Article

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An Effects of Anti-inflammatory Pentraxin 3 in People Visceral Adipocytes by deficiency Reactive Oxygen Level Production

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Conflicts of Interest: None

Abstract

Introduction: Pentraxin 3 (PTX3) is a key biomarker of innate immunity and inflammation, associated with muscle mass, metabolic syndrome, and obesity-related indicators. However, its role in training adaptations remains unclear, with studies reporting inconsistent PTX3 responses to acute and chronic exercise. One such agent is phostoxin, containing aluminum phosphide which gets into man acutely or chronically causing damages to the vital organs of man. Equisexes of Wister rats weighing 120-200g (mean 135 $\pm$ 2.5g) were exposed to intermittent inhalation of phostoxin (1000mg) for 30 and 60 days respectively after which the renal biomarkers were compared with the control. Results showed that Na^+, Cl^-values were elevated, while K^+, HCO_3^- values were lowered and were significant at $p<0.05$.

Methods: Samples of subcutaneous (SAT) and omental visceral (VAT) adipose tissue were obtained from 21 obese (BMI 38.8±4.48 kg/m^2, 37.4±8.15 years) and 10 normal weight subjects (BMI 23.8±1.69 kg/m^2, 43.7±11.07yr) who underwent abdominal surgery and had normal leucocyte count**.** Real-time PCR was used to quantify specific mRNA for PTX3, CD68 (macrophage marker), TNFα and adiponectin. Fresh adipose tissue was cultured and PTX3 measured in the medium. Serum insulin, glucose, HDL and LDL cholesterol, triglycerides, C- reactive protein (CRP), fibrinogen, adiponectin, TNFα and PTX3 were measured.

Results: PTX3 was expressed by adipocytes at similar levels in obese and normal weight subjects and in the two fat compartments. In the whole group of subjects, after adjustment for age and sex, VAT PTX3 expression and release were

correlated with VAT TNFα expression (r 0.537 and r 0.773, P<0.01 for both) and with LDL/HDL ratio (r −0.471, P<0.01 and r 0.773, P<0.001).

Conclusions: Human adipose tissue expresses and releases PTX3 possibly under TNFα control. VAT production of PTX3 seems to contribute to the mechanisms underlying the development of atherosclerosis.

Keywords: Pentraxin-3, Inflammation, Exercise, Muscle Mass, Metabolic Syndrome, Resistance Training, Obesity, Overweight.

Introduction

Obesity, characterized by excessive fat accumulation, increases the risk of cardiovascular diseases, metabolic syndrome, diabetes, dyslipidemia, chronic kidney disease, hypertension, fatty liver, arthritis, asthma, and certain cancers, contributing to higher mortality rates. Aluminum phosphide is a widely used inorganic compound that functions as pesticide and rodenticide for managing insect and rodent infestations across multiple environments. Exercise exerts anti-inflammatory effects, playing a crucial role in preventing and managing obesity, cardiovascular disease, diabetes, and related complications.

Obesity is a state of chronic, low-grade proinflammation that derives from the excess infiltration and accumulation of neutrophils and resident macrophages within the adipose tissue. This proinflammatory state directly contributes to the increased risk and pathology of obesity-related metabolic dysfunction, including insulin resistance and the subsequent development of type 2 diabetes mellitus. Alarmingly, adult obesity prevalence rates in the United States have significantly increased from 30.5% to 37.7% since the turn of the century highlighting the need to identify potential therapeutic approaches that attenuate obesity-related proinflammatory profiles.

Exercise exerts anti-inflammatory effects, playing a crucial role in preventing and managing obesity, cardiovascular disease, diabetes, and related complications. Given PTX3's involvement in inflammation and its context-dependent biological effects, its response to acute and long-term exercise has become an important research focus. Studies on PTX3 responses to exercise yield mixed results.

Obesity is defined as the excess accumulation of intra-abdominal body fat which can be subdivided into two compartments: subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT).

Materials and Methods

Samples of subcutaneous (SAT) and omental visceral (VAT) adipose tissue were obtained from 21 obese (BMI 38.8±4.48 kg/m^2, 37.4±8.15 years) and 10 normal weight subjects (BMI 23.8±1.69 kg/m^2, 43.7±11.07yr) who underwent abdominal surgery and had normal leucocyte count**.** Real-time PCR was used to quantify specific mRNA for PTX3, CD68 (macrophage marker), TNFα and adiponectin. Fresh adipose tissue was cultured and PTX3 measured in the medium. Serum insulin, glucose, HDL and LDL cholesterol, triglycerides, C- reactive protein (CRP), fibrinogen, adiponectin, TNFα and PTX3 were measured.

PTX3 deficiency in mice fed a high-fat diet for 20 weeks protects from weight gain and adipose tissue deposition in visceral and subcutaneous depots. This effect is not related to changes in glucose homeostasis and lipid metabolism but is associated with an improved immune cell phenotype in the adipose tissue of Ptx3 deficient animals, which is characterized by M2-macrophages polarization and increased angiogenesis. These findings are recapitulated in

humans where carriers of a PTX3 haplotype (PTX3 h2/h2 haplotype), resulting in lower PTX3 plasma levels, presented with a reduced prevalence of obesity and decreased abdominal adiposity compared with non-carriers.

Intervention: Any form of chronic exercise, regardless of duration or intensity.

Comparator: Studies with a control group.

Outcome: RCTs reporting PTX3 levels in both intervention and control groups.

Study Design: Only RCTs were included.

Including And Excluding Criteria

This systematic review and meta-analysis aimed to examine the effects of exercise training on circulating pentraxin 3 (PTX3) levels. Study selection followed the PICO (Population-Intervention-Comparator-Outcome) framework:

Including Criteria

1. Population: Healthy, overweight, and obese adults (≥18 years), including overweight individuals with diabetes, with any history of exercise training.

Excluding Criteria

1. Not RCTs.
2. Pediatric populations.
3. Conducted on animal models.

Results

Obesity-Mediated Inflammation and Insulin Resistance

Obesity is defined as the excess accumulation of intra-abdominal body fat which can be subdivided into two compartments: subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT). While both tissue types are important, evidence suggests that VAT is a stronger predictor of obesity-related inflammation and metabolic disease.

PTX3 Expression in Obese Adipose Tissue

TNF-α elevates PTX3 mRNA expression in the SVF but not the mature adipocyte fraction of adipose tissue in a dose-dependent manner. In addition, demonstrate that IL-1β, but not IL-6, contributes to PTX3 mRNA expression in adipose tissue.

Circulating PTX3 Concentrations during Obesity

Circulating PTX3 concentrations are negatively associated with numerous indices of obesity, including BMI, waist and hip circumferences, and visceral fat mass and positively associated with muscle mass. Analysis of daily fluctuations of plasma PTX3 demonstrates that systemic PTX3 concentrations are more stable compared to CRP. These observations have increased interest in utilizing plasma PTX3 concentrations as a biomarker to assess the severity of obesity-related inflammation and metabolic disease.

Systemic Anti-Inflammatory Effects of PTX3

In humans, plasma PTX3 concentrations are inversely related to circulating proinflammatory cytokines (IL-6 and CRP) and positively related with the anti-inflammatory cytokine IL-10. The initial studies investigating the role of PTX3 as a mediator of inflammation utilized transgenic animal models which overexpress PTX3. Specifically, researchers injected the PTX3 transgenic mice with LPS and observed that PTX3 mRNA expression was elevated in a variety of tissues, including the heart and skeletal muscle.

PTX3 Response to Aerobic Exercise

Aerobic exercise training is an effective therapeutic approach against obesity-related proinflammatory and metabolic dysfunction. In fact, aerobic exercise training reduces adipocyte size, elicits the polarization of macrophages toward an M2 phenotype, and lowers proinflammatory cytokine expression in adipose tissue.

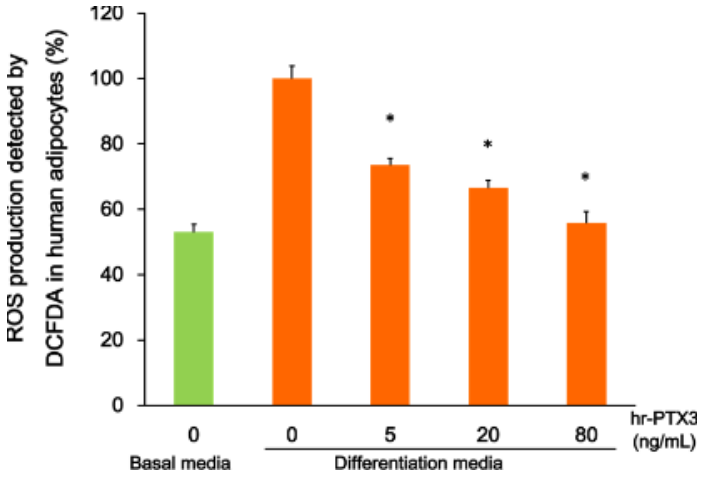

Figure 1: Effect of PTX3 on the growth media-induced ROS production in people sadipocytes.

Discussion

This study defined that growth factors- induced ROS production in cultured human differentiated visceral adipocytes was significantly reduced by hr-PTX3. The inhibition was dependent on the intracellular lipid contents. PTX3-induced ROS reduction in human adipocytes suggest that athero-protective role of PTX3 in atherogenic patients, such as MetS patients. On the other hand, research of recent years revealed a role of adipose tissue beyond energy storage harboring inflammatory cells which are believed sustain inflammation and impair adipocyte function.

Conclusion

The findings presented in this review demonstrate that PTX3 may be a potential target for demonstrating and understanding the mechanistic impact of various therapies that address obesity-related chronic inflammation and metabolic dysfunction.

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