Metabolic Control By Palmitoylethanolamide (PEA) In An Animal Model Of Diet-Induced Obesity (DIO)

F. Di Guida[1], A. Santoro[1], A. Lama[1], C. Pirozzi[1], R. Russo[1], A. Calignano[1], G. Mattace Raso[1], R. Meli[1]

[1]Dept. of Pharmacy, University of Naples Federico II

Fatty acyl ethanolamides are a class of endogenous lipid molecules with different long-chain fatty acids, and are generally referred to as N-acylethanolamines (NAEs) (Schmid et al., 1990; Hansen et al., 2000). Among NAEs N-palmitoylethanolamide (PEA) is gaining ever-increasing interest (Hansen, 2010) not only for its anti-inflammatory and analgesic effects (Lo Verme et al., 2005), but also for its novel metabolic activity mediated by peroxisome-proliferator activated receptor α (PPAR-α) (Mattace Raso et al., 2014). Obesity is a complex, chronic disease and results from an imbalance of food intake, basal metabolism and energy expenditure (Wang and Liao, 2012) modulate by endogenous lipid mediators.

The aim of this study was to investigate the effect of PEA on the prevention of metabolic alterations, occurring in diet-induced obesity (DIO) in mice. After weaning, young mice (were randomly divided into four groups (at least 10 animals for each group) as follows: 1) control group (STD) receiving chow diet and vehicle per os by gavage; 2) STD group treated with PEA (STD+PEA, 30 mg/kg/die per os); 3) DIO group receiving vehicle; 4) DIO group treated with PEA (DIO+PEA, 30 mg/kg/die per os). The treatments started after 12 weeks of feeding with DIO and continued for 10 weeks. During the experimental period body weight and blood pressure were monitored. One week before sacrifice, all mice were subjected to the oral glucose tolerance test (OGTT) and insulin tolerance test (ITT). OGTT was performed in 12h fasted animals, which received oral glucose (1g/kg) and glycemia was measured at 30, 60, 90 and 120 minute. ITT was performed with mice fed ad libitum. After determination of basal blood glucose levels, each animal received an intraperitoneal injection of insulin, 0.75 U/kg. Blood glucose levels were measured at 15, 30, 60, 90 and 120 min after insulin injection. At the end of the experimental protocol, before sacrifice, bioelectrical impedance analysis was applied to determine fat body composition. Hormonal and biochemical markers were also evaluated in serum.

As expected, DIO feeding induced insulin-resistance and PEA treatment prevented its onset. We also showed that PEA caused a reduction of body weight, fat mass and blood pressure and an improvement of glucose levels in OGTT and ITT in treated mice compared to DIO. PEA effects on serum biochemical and inflammatory parameters underlined a marked reduction of ALT, AST, cholesterol and proinflammatory cytokines such as TNF-α, IL-1 and MCP-1. Furthermore, PEA normalized serum levels of metabolic hormones significantly increasing adiponectin and decreasing leptin and HOMA-IR index.

In conclusion, we proved that PEA prevented biochemical alterations and glycidic imbalance, limiting the inflammatory process underpinned to obesity induced by high fat diet. Our data also indicate that oral administration of PEA can be considered a valid 'MULTI TARGET' therapeutical strategy to prevent or limit obesity and related metabolic complications.