

Impact of metformin and exercise, isolated or associated, on morphology and oxidative stress in adipose tissue of a polycystic ovary syndrome rat model

R R Marcondes (BR) [1], T H Gonçalves (BR) [2], G S Araújo (BR) [3], B A Guerra (BR) [4], M A Mori (BR) [5], G D Maffazioli (BR) [6], I L Gomes-Santos (BR) [7], C E Negrão (BR) [8], K C Carvalho (BR) [9], E C Baracat (BR) [10], G A Maciel (BR) [11]

Context: Adipose tissue dysfunction, such as adipocyte hypertrophy and inflammation, is a metabolic characteristic found in women with polycystic ovary syndrome (PCOS). Adipocyte hypertrophy is strongly correlated to insulin resistance in PCOS patients. Exercise and metformin have been shown positive effects on metabolic features of PCOS. However, the mechanisms behind benefits of these therapies to women with PCOS are largely unknown.

Objective: The aim of this study was to investigate the impact of exercise (Ex) and metformin (Met), associated or alone, on adipocyte morphology and oxidative stress in the inguinal and mesenteric fat of a PCOS rat model.

Methods: Female rats with 2 days of age received a single sc injection of testosterone propionate (1.25 mg) to induce PCOS-like phenotype. Controls (Con) received a single injection of vehicle. At 80 days of age treatments with Ex and/or Met started and groups were sorted as follows: 1) Con; 2) PCOS; 3) PCOS+Ex; 4) PCOS+Met; and 5) PCOS+Met+Ex. Exercise was performed in a treadmill at 60% of VO₂max 5 days/week. Metformin (50 mg/kg) was given orally by gavage. Body weight, food intake, and exercise capacity were evaluated. After 6 weeks of treatments, the rats were euthanized and inguinal and mesenteric fat depots were dissected and stored for morphometric and oxidative stress analyses.

Animals: Female Wistar rats

Interventions: PCOS rat models were treated with Ex and/or Met.

Main Outcome Measures: Morphometric analysis of adipocytes and oxidative stress in the adipose tissue.

Results: All PCOS groups have higher body weight than Con ($P < 0.001$). There were no effects of Ex and/or Met on body weight in PCOS rat models. Food intake did not differ among groups. PCOS group presented increased size of mesenteric adipocytes compared to controls ($P < 0.01$). Association of Met with Ex (PCOS+Met+Ex group), but not Ex or Met alone, decreased significantly the size of mesenteric adipocytes compared to untreated PCOS rat models ($P < 0.001$). There was a tendency to increased levels of oxidized and reduced glutathione in the mesenteric fat of untreated PCOS rat models.

Conclusions: The association of Met with Ex, but not Met or Ex alone, normalized adipocyte hypertrophy in mesenteric fat of PCOS rat models. The association of Met with Ex might be helpful to treat metabolic impairments in the adipose tissue of women with PCOS.

[1] Faculdade de Medicina da Universidade de São Paulo, [2] Faculdade de Medicina da Universidade de São Paulo, [3] Faculdade de Medicina da Universidade de São Paulo, [4] Universidade Estadual de Campinas, [5] Universidade Estadual de Campinas, [6] Faculdade de Medicina da Universidade de São Paulo, [7] Harvard Medical School, [8] Faculdade de Medicina da Universidade de São Paulo, [9] Faculdade de Medicina da Universidade de São Paulo, [10] Faculdade de Medicina da Universidade de São Paulo, [11] Faculdade de Medicina da Universidade de São Paulo