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PPAR- γ ACTIVATION RESTORES LIVER INFLAMMATION AFTER CHRONIC EXERCISE IN PPAR- α KNOCKOUT OBESE MICE.

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BACKGROUND

Inflammation has exhibit a straight correlation to nonalcoholic steatohepatitis (NASH). Chronic moderate exercise is one of the main treatments for NASH by decreasing hepatic pro-inflammatory cytokines and activating PPARs family⁽¹⁾. PPAR- α and γ are the most common isoforms expressed in liver. PPAR- γ plays key anti-inflammatory role decreasing NF- κ B activity and promoting M2 macrophages polarization, whereas PPAR- α acts modulating the transcription of enzymes involved in β -oxidation, favoring fatty acid oxidation ⁽²⁾. Obese PPAR- α knockout (KO) mice exhibit low liver lipid accumulation but increases liver inflammation when trained, followed by a reduction in PPAR- γ protein and gene expression ⁽³⁾. So here, we investigated whether rosiglitazone treatment (PPAR- γ activation) could restores liver inflammation after chronic exercise in PPAR- α knockout obese mice.

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METHODS

PPAR- α KO mice were fed with high fat diet (HF, 59% fat) during 12 weeks, and allocated in 3 groups: 1) HF-KO (remained sedentary); 2) HFT-KO (submitted chronic moderate training on a treadmill during the last 8 weeks; and 3)HFT-RG-KO (submitted chronic exercise training and had 15mg/kg/day of oral rosiglitazone during the last 8 weeks). We evaluated lipid profile, cytokines (ELISA) and gene expression (RT-PCR) in the liver.

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RESULTS

Rosiglitazone was efficient in reversing PPAR- α knockout mice Insulin resistance and decreased free fatty acid in serum. The protein expression of pro-inflammatory cytokines (IL-1 β , IL-6, TNF- α , MCP-1) and NF- κ B and IL-1 β mRNA were decreased in HFT-RG-KO comparing to HFT-KO indicating low liver inflammation. Although PPAR- γ mRNA were not modified, its target genes (PGC-1 α and FAS) were higher to HFT-RG-KO compared to HFT-KO implying PPAR- γ activation. F4/80 expression was reduced in both exercise groups, and CD86 gene expression had a decrease only in HFT-RG-KO suggesting M2 polarization.

CONCLUSIONS

Rosiglitazone treatment was efficient to induce PPAR- γ activation leading to low liver inflammation after chronic exercise in PPAR- α knockout obese mice.

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