Abstract: P310

A new dual-PPAR agonist (GQ-11), prevents ischemia-reperfusion damage in rats after supraceliac aorta clamping

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INTRODUCTION: Ischemia-Reperfusion (I/R) is defined as a pathological condition characterized by restriction of blood supply followed by flow restoration and subsequent re-oxygenation, representing the major challenge during organ transplantation and general cardiothoracic surgery. Either ischemia and reperfusion have been associated to inflammation and oxidative stress induction, promoted by HIF, TNFα, NFκB and IL6 imbalance as well as ROS formation. Nevertheless, the actual pharmacological approach to prevent I/R damage has so far been unsuccessful. As PPARγ agonists have been described as transcription factors related to anti-inflammatory markers, here we propose to analyze the effects of a new thiazolidine compound, GQ-11, in I/R.

AIMS: To investigate GQ-11 effects in I/R-related damage.

METHODS: Male Wistar rats were pre-treated by gavage with Vehicle (NaCl 0.9% Tween 0.25%), commercial PPARγ agonist (10 mg/kg) or GQ-11 (10 mg/kg) for 7 days and submitted to supraceliac aorta clamping for 30 minutes and 3 hours reperfusion. Positron Emission Tomography (PET) was performed observing 18F-FDG uptake in liver and bowel area in a microPET (Albira, Carestream Health) for 15 minutes imaging acquisition. Organs and blood were analyzed by RT-PCR and Western Blot.

RESULTS: 18F-FDG uptake was decreased - qualitative and quantitative (SUVmax) - in liver and bowel of animals treated with GQ-11 when compared to animals treated with commercial PPARγ agonist or controls. The treatment also modulated IL6, IL1b, IL10, TNFα, TGFβ, CCL2 and Mt1 indicating inflammation/oxidative stress modulation to I/R damage protection.

CONCLUSION: Regulation of both inflammation and oxidative stress seems to be an important target in the search for I/R management, suggesting that PPAR agonists - including GQ-11 - might be important mediators in these conditions.