

ROSIGLITAZONE REDUCES INFLAMMATORY EVENTS IN RAT VASCULAR INJURY

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We previously found that several inflammatory markers, e.g., nuclear factor- κ B (NF- κ B), were increased and a neointima was formed in a model of carotid surgical injury (1). Several *in vivo* studies have shown that various peroxisome proliferator-activated receptor- γ (PPAR- γ) agonists, like rosiglitazone, may participate in the control of inflammation by modulating the production of inflammatory mediators, the coagulation cascade and they are able to inhibit hyperplasia and restenosis after balloon-mediated vascular injury in rats (2). The purpose of the present study was to determine if chronic treatment with rosiglitazone protects rat carotid artery from surgical injury induced by an incision of the vascular wall. To this aim we measured COX-2, NF- κ B, platelet aggregation and neointima formation in rats administered rosiglitazone (10 mg/kg/die, by gavage) for 7 days before carotid injury and 21 days after injury. Control rats received physiological solution. Already after 7 days from injury COX-2 expression, evaluated by western blot, was significantly lower in the treated carotid versus controls ($p < 0.001$) and this reduction was observed until 21 days after injury ($p < 0.0005$). Rosiglitazone also caused a significant decrease of NF- κ B/DNA binding activity, evaluated by electrophoretic mobility shift assay, in nuclear extracts of treated carotids at all time points considered. Platelet aggregation was reduced by $\pm 30\%$ in treated versus control carotids ($p < 0.0005$). The influx of inflammatory cells in response to injury, monitored by electron microscopy and immunohistochemistry, was lower in treated than in control carotids starting 7 days after rosiglitazone treatment. Our results indicate that rosiglitazone exerts an anti-inflammatory and anti-proliferative effect suggesting a potential therapeutic role in atherosclerotic vascular disease.

1. Rinaldi B., Romagnoli P., Bacci S., Carnuccio R., Maiuri MC., Donniacuo M., Capuano A., Rossi F. and Filippelli A. (2006) *Br J Pharmacol* 147: 175-182
2. Soo L., Cheng JJ., Min K., Sung SC., Ho SP., In Kyu L., Choon TL., Young MC., Hong KL. and Kyong SP. (2006) *Biol* 26: 808-813