Pentoxifylline treatment alleviates kidney ischemia/reperfusion injury: Novel involvement of galectin-3 and ASK-1/JNK & ERK1/2/NF-əB/HMGB-1 trajectories

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Abstract

Despite the documented renoprotective effect of pentoxifylline (PTX), a non-selective phosphodiesterase-4 inhibitor, the studies appraised only its anti-inflammatory/-oxidant/-apoptotic capacities without assessment of the possible involved trajectories. Here, we evaluated the potential role of galectin-3 and the ASK-1/NF-əB p65 signaling pathway with its upstream/downstream signals in an attempt to unveil part of the cascades involved in the renotherapeutic effect using a renal bilateral ischemia/reperfusion (I/R) model. Rats were randomized into sham-operated, renal I/R (45 min/72 h) and I/R + PTX (100 mg/kg; p.o). Post-treatment with PTX improved renal function and abated serum levels of cystatin C, creatinine, BUN and renal KIM-1 content, effects that were reflected on an improvement of the I/R-induced renal histological changes. On the molecular level, PTX reduced renal contents of galectin-3, ASK-1 with its downstream molecule JNK and ERK1/2, as well as NF-əB p65 and HMGB1. This inhibitory effect extended also to suppress neutrophil infiltration, evidenced by diminishing ICAM-1 and MPO, as well as inflammatory cytokines (TNF-Ŭ/IL-18), oxidative stress (MDA/TAC), and caspase-3. The PTX novel renotherapeutic effect involved in part the inhibition of galectin-3 and ASK-1/JNK and ERK1/2/NF-əB/HMGB-1 trajectories to mitigate renal I/R injury and to provide basis for its anti-inflammatory, antioxidant, and anti-apoptotic impacts.

Journal of Pharmacological Science 2021, July