

Cortistatin-14 Represses Oxidative-Inflammatory Signaling via Regulation of MicroRNA-200c and HDAC6 in Rhabdomyolysis-Provoked Acute Kidney Injury

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SUMMARY. Rhabdomyolysis provoked acute kidney injury (RPAKI) is a high-risk syndrome with fatal renal complications. The present work is targeted to ascertain the beneficial effects of cortistatin-14 (C14) against glycerol-induced RPAKI in mice. We observed that C14 down-modulated the oxidative stress and inflammation through the dual inhibition of microRNA-200c (miR-200c) and histone deacetylase 6 (HDAC6) in the renal tissues of RPAKI mice. Treatment with C14 prevented the leakage of creatine kinase (CK) into the bloodstream against glycerol-induced RPAKI. Of note, suppression of superoxide dismutase (SOD) and surge in malondialdehyde (MDA) levels were effectively counteracted by C14 treatment against RPAKI. Besides, C14 treatment displayed potential anti-inflammatory effect in relation to the inhibitory action on the expression of caspase-1, nuclear factor-kappa B (NF- κ B), tumor necrosis factor alpha (TNF- α) and interleukin 1 beta (IL-1 β). Attenuation of oxidative/inflammatory stress implies that C14 might accord muscular/renal protection against rhabdomyolysis and associated nephrotoxicity.

RESUMEN. La rabdomiólisis provocada por una lesión renal aguda (RPAKI) es un síndrome de alto riesgo con complicaciones renales fatales. El presente trabajo está dirigido a determinar los efectos beneficiosos de la cortistatina-14 (C14) contra el RPAKI inducido por glicerol en ratones. Observamos que C14 modulaba el estrés oxidativo y la inflamación mediante la inhibición dual de microRNA-200c (miR-200c) e histona desacetilasa 6 (HDAC6) en los tejidos renales de ratones RPAKI. El tratamiento con C14 evitó la fuga de creatina quinasa (CK) en el torrente sanguíneo contra RPAKI inducido por glicerol. Es de destacar que la supresión de la superóxido dismutasa (SOD) y el aumento de los niveles de malondialdehído (MDA) fueron efectivamente contrarrestados por el tratamiento con C14 contra RPAKI. Además, el tratamiento con C14 mostró un posible efecto antiinflamatorio en relación con la acción inhibitoria sobre la expresión de caspasa-1, factor nuclear-kappa B (NF- κ B), factor de necrosis tumoral alfa (TNF- α) e interleucina 1 beta (IL-1 β). La atenuación del estrés oxidativo / inflamatorio implica que C14 podría otorgar protección muscular / renal contra la rabdomiólisis y la nefrotoxicidad asociada.

KEY WORDS: acute kidney injury, cortistatin-14, HDAC6, microRNA-200c, rhabdomyolysis.

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