TREATMENT WITH CURCUMINE DECREASES RENAL DAMAGE ASSOCIATED WITH RHABDOMYOLYSIS - ACUTE KIDNEY INJURY

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INTRODUCTION AND AIMS: Muscledamage (rhabdomyolysis) releases myoglobin into the bloodstream and may induce acute kidney injury (AKI). Once filtered by the kidney, myoglobin causes oxidative stress, tubular death and endothelial damage. There is no specific treatment for rhabdomyolysis, only palliative care. Curcumin, a compound from the Curcuma longa, is a powerful antioxidant because of its inducer effect on NrF2 (Nuclear factor (erythroid-derived 2) -like 2). The purpose of this study is to analyse the possible beneficial effect of curcumin in the prevention of renal damage associated with rhabdomyolysis.

METHODS: We performed an experimental model of AKI associated to rhabdomyolysis by the intramuscular injection of 50% glycerol (10mg/kg of weight) in 12-week-old male C57BL/6 mice. Curcumin was injected intraperitoneally (1mg/kg) two times: the day before and the same day of the injection of glycerol. Animals were sacrificed at 24 hours post-injection of glycerol. Blood and kidney samples were collected to perform gene expression studies by Real Time-PCR and protein expression by western blot and immunohistochemistry. In addition, we carried out studies in murine tubular cells (MCTs) to study the molecular mechanisms involved in the protection of curcumin.

RESULTS: Mice with rhabdomyolysis showed alteration of renal function (increase in urea and creatinine serum levels), and histological damage (tubular death and tubular lumen dilatation, loss of brose border, oedema). In line with these results, we observed an increase in the gene expression of markers of tubular (NGAL and KIM-1) and endothelial (ICAM-1 and endothelin) damage, as well as enhanced expression of proinflammatory cytokines (CCL2 and TNF-α), induction of catabolism of the heme group (HO-1 and ferritin), oxidative stress (production of MDA and decreased GSH content) and cell death (TUNEL). All these effects were partially reversed in the group of mice treated with curcumin. In tubular cells, the administration of curcumin induced the activation of NrF2 and HO-1, the enzyme that degrades the heme group. In line with these results, administration of curcumin decreased the production of inflammatory mediators (CCL2, IL-6 and TNF-α), cell death and the production of reactive oxygen species in cells stimulated with myoglobin. These protective effects were mediated, almost partially, by HO-1 since treatment with S6P, an HO-1 inhibitor, abolished the curcumin-mediated protection.

CONCLUSIONS: Curcumin reduces renal damage associated with rhabdomyolysis, so this compound could be a possible therapeutic approach for patients with this pathology.