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Effect of betaine supplementation on cisplatin-induced nephrotoxicity in experimental animals: Contribution of nuclear factor kappa and caspase-3

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Abstract

Cisplatin is widely used in the treatment of solid tumors. Nevertheless, its full clinical utility is limited due to some adverse side effects including renal toxicity. This study aims to investigate the effect of betaine supplementation on the extent of tissue damage in cisplatin-induced nephrotoxicity. The animals were divided into four groups (n=8 per group): control, betaine, cisplatin (CDDP), and betaine + cisplatin. (1) saline control group; (2) cisplatin group in which rats were injected with a single intraperitoneal injection of cisplatin (5 mg/kg); (3) betaine group, in which betaine was given at a dose of (250 mg/kg/day) orally via gavage for 21 days; (4) cisplatin + betaine group in which betaine was given (250 mg/kg/day) orally via gavage for 21 days prior to cisplatin injection and daily for 5 days after cisplatin. At the end of experiments, the animals were sacrificed; blood and kidneys were collected. Nephrotoxicity was indicated by measuring blood urea nitrogen and serum creatinine levels. Renal content of malondialdehyde (MDA), an indicator of lipid peroxidation was elevated. The contents of internal antioxidants; reduced glutathione, glutathione peroxidase, catalase and superoxide dismutase were declined in renal tissues. Renal tumor necrosis factor-α (TNF- α) and caspase-3 were elevated in cisplatin-treated animals. Nuclear factor–kappa and caspase-3 were up-regulated in renal tissues as indicated by immunohistochemical analysis. Hisopathological changes were observed in cisplatin group. Betaine supplementation was able to protect against deterioration in kidney function, abrogate the decline in antioxidants enzymes and suppressed the increase in MDA and TNF- α concentrations. Moreover, betaine inhibited nuclear factor–kappa and caspase-3 activation and improved the histological changes induced by cisplatin. Betaine could be a beneficial dietary supplement to attenuate oxidative stress induced by cisplatin nephrotoxicity.