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Effects of sodium nitrite on renal damage induced by renovascular hypertension

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Renovascular hypertension, characterized by increased oxidative stress and reduced nitric oxide (NO) bioavailability, represents a pathophysiological state with detrimental effects on kidney function. Nitrite, a metabolite involved in the NO cycle, has emerged as a potential therapeutic agent due to its ability to generate NO and exert antioxidant effects. However, the specific renal effects of sodium nitrite in the context of two-kidney, one-clip (2K1C) hypertension remain to be elucidated. This study aimed to evaluate the impact of sodium nitrite administration on renal injury associated with 2K1C hypertension.

Hypertension was induced in male Wistar rats via unilateral clipping of the left renal artery, creating the 2K1C model. Two weeks post-surgery, animals were orally treated (via gavage) with sodium nitrite at two doses: 1 mg/kg/day and 15 mg/kg/day, or a vehicle control, for four weeks. Blood pressure (BP) was measured weekly using tail-cuff plethysmography. Renal function was assessed by measuring plasma urea and creatinine levels. To investigate oxidative stress, catalase (CAT) and superoxide dismutase (SOD) enzyme activities were quantified, along with levels of reduced glutathione (GSH), lipid peroxidation, and superoxide anion (O_2^-).

Sodium nitrite treatment at 15 mg/kg/day significantly reduced systolic BP in hypertensive 2K1C rats compared to untreated rats ($p<0.05$, C:126.7±3.677; H:170.5±6.542; H15:162.4±6.712). Additionally, renal function, indicated by plasma urea and creatinine concentrations, markedly improved with the higher nitrite dose (urea $p<0.05$; C:36.71±4.553; H:76.37±24.53; H15:47.82±13.86; creatinine $p<0.05$; C:0.430±0.0600; H:0.540±0.105; H15:0.3550±0.117). In terms of oxidative stress markers, SOD activity was significantly reduced in untreated hypertensive rat kidneys ($p<0.05$, C:0.7176±0.06426; H:0.636±0.0888; H1:0.703±0.0866; H15:0.648±0.173). CAT activity, which was impaired in 2K1C rats (0.2772±0.1837 U/mg protein), recovered with nitrite at the higher dose (CAT $p<0.05$, C:0.651±0.255; H:0.2772±0.1837; H15:0.6654±0.1440). A significant reduction in GSH levels was observed in hypertensive rats (C:44.80±10.59), but these levels were restored following nitrite treatment (H15:44.25±10.07). Lipid peroxidation, a marker of oxidative damage, was elevated in 2K1C rats but reduced by treatment with 15 mg/kg/day nitrite ($p<0.05$, C:0.314±0.158; C15:0.361±0.087; H:0.497±0.113; H15:0.278±0.084). Superoxide anion (O_2^-) levels, which increased with hypertension ($p<0.05$, C:3.695±0.9245; C15:0.3999±0.1667;

H:3.844±1.598; H1:0.9643±0.2063; H15:0.4431±0.1838), significantly decreased in all nitrite-treated groups.

These findings suggest that sodium nitrite exerts renoprotective effects in 2K1C-induced hypertension through its antioxidant activity. Treatment with 15 mg/kg/day sodium nitrite effectively mitigated oxidative stress by restoring CAT and GSH levels, decreasing lipid peroxidation, and reducing superoxide anion concentrations. These improvements translated into enhanced renal function and lowered blood pressure. The results highlight the potential of sodium nitrite as a therapeutic agent for the treatment of renovascular hypertension and prevention of hypertension-induced renal damage. Further studies are needed to explore its long-term efficacy and mechanistic pathways.

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