N-ACETYLCYSTEINE AMELIORATE HEAT STROKE INDUCED ACUTE KIDNEY INJURY

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Background

The heat-related illness has become more prevalent and contributed to increased morbidity and mortality in the world with global warming. Heat stroke (HS) is the most severe and potentially fetal heat-related illness. However, specific and effective therapeutic strategies are not yet available to date. Heat stress is known to generate ROS which play a central role in disease process leading to multiple organs damage including acute kidney injury (AKI). We assessed the efficacy of N-acetylcysteine (NAC), a thiol-containing free radical scavenger and antioxidant, therapy for HS induced AKI.

Methods

Adult male Sprague-Dawley rats, weight between 325 ± 15 g (age 9~10 weeks) exposed to a Ta of 40°C under anesthesia in pre-warming chamber (with relative humidity of 55%) for 60 mins were performed to induce experimental HS. The rats are randomly allocated into four groups. Two experimental HS groups of rats pre-treated with either saline, or NAC and another two control groups of rats treated identically kept at room temperature of 24.0°C used as normothermic controls. Oral NAC, 10mg/mL, in drinking water was used. All physiological and biochemical variables are measured during the observation. Disease severity was verified by with serum and urine metabolic profiles and with renal histopathology. The expression of cytokines and oxidative stress markers, cell apoptosis, and the associated mechanisms were also determined.

Result

HS rat treated with NAC displayed a better survival rate and the hemodynamics were more stable including body temperature, mean arterial pressure and heart rates. NAC also significantly ameliorate reduce severity of AKI based on biochemical (levels of blood urea nitrogen, creatinine) and histopathlogical evidence. The NGAL-positive cells and TUNEL-positive apoptotic cells in the kidney were also significantly reduced in theNAC-treated HS rat. Oxidative stresses markers (Advanced Oxidation Protein Products, AOPP and Malondialdehyde, MDA) in the serum were significantly reduced in NAC -treated HS rat. Cytokines studies indicated that NAC significantly modulate serum proinflammatory, and anti-inflammatory cytokines. The effect on other organs revealed similar pattern as kidney.

Fig. 1 Effects of heat stress on Tc, MAP and HR

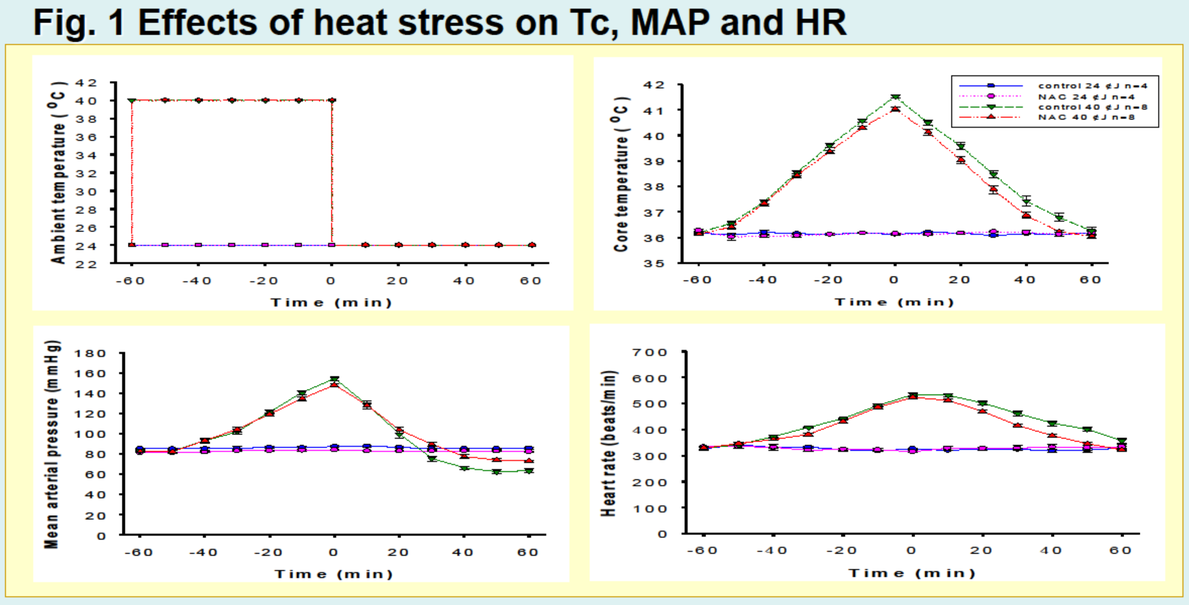


Fig. 2 Effects of NAC on survival in mice with HS induced AKI

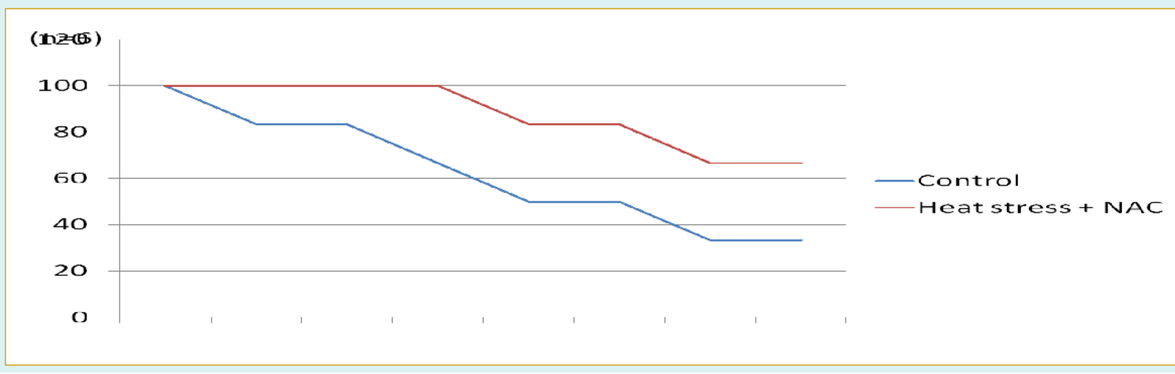
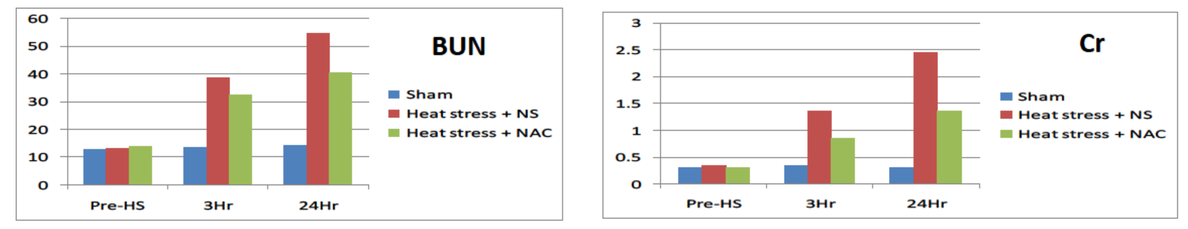


Fig. 3 Effects of NAC on renal function in mice with HS induced AKI



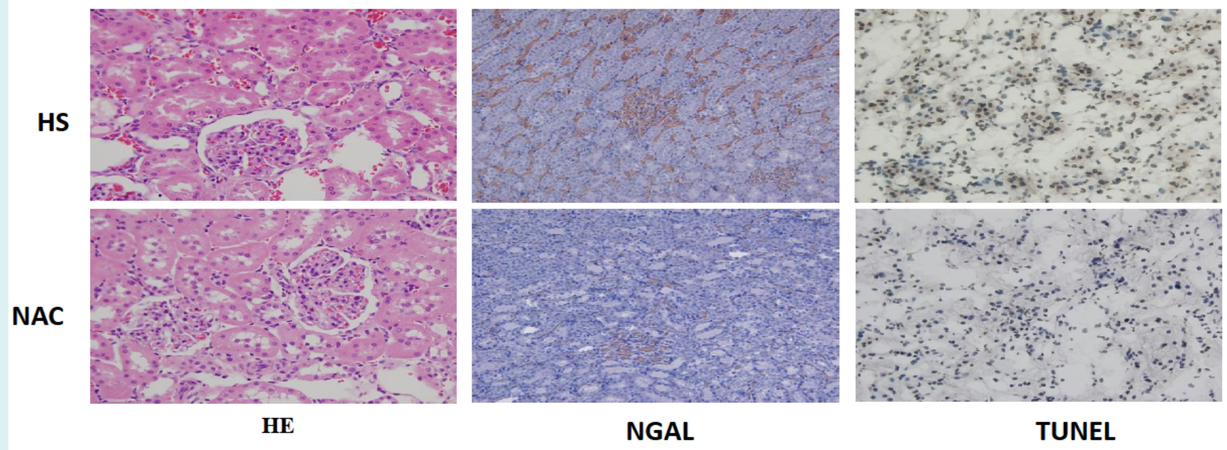


Fig. 4 Effects of NAC on serum biochemistries in mice with HS induced AKI

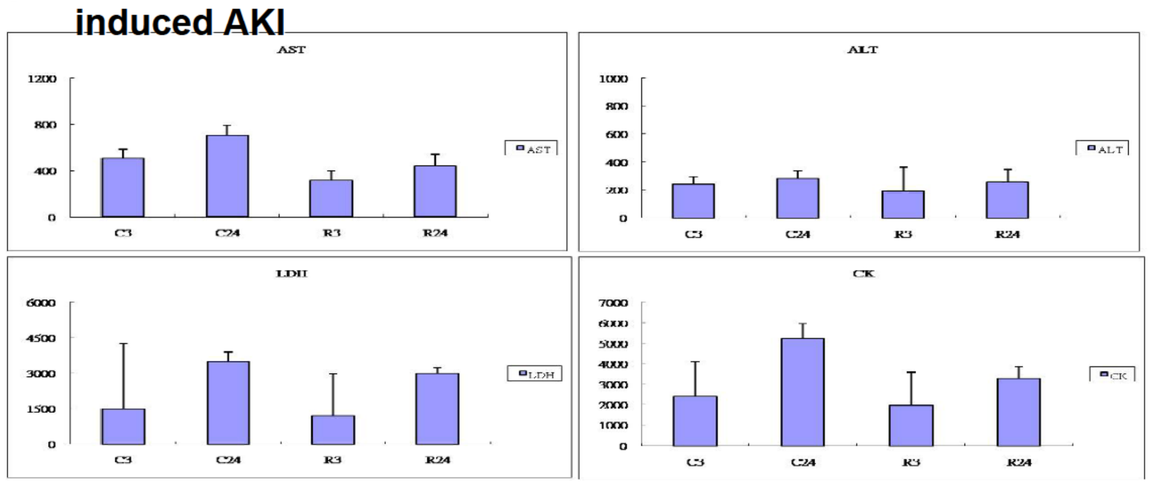


Fig. 5 Effects of NAC on oxidative markers in mice with HS induced AKI

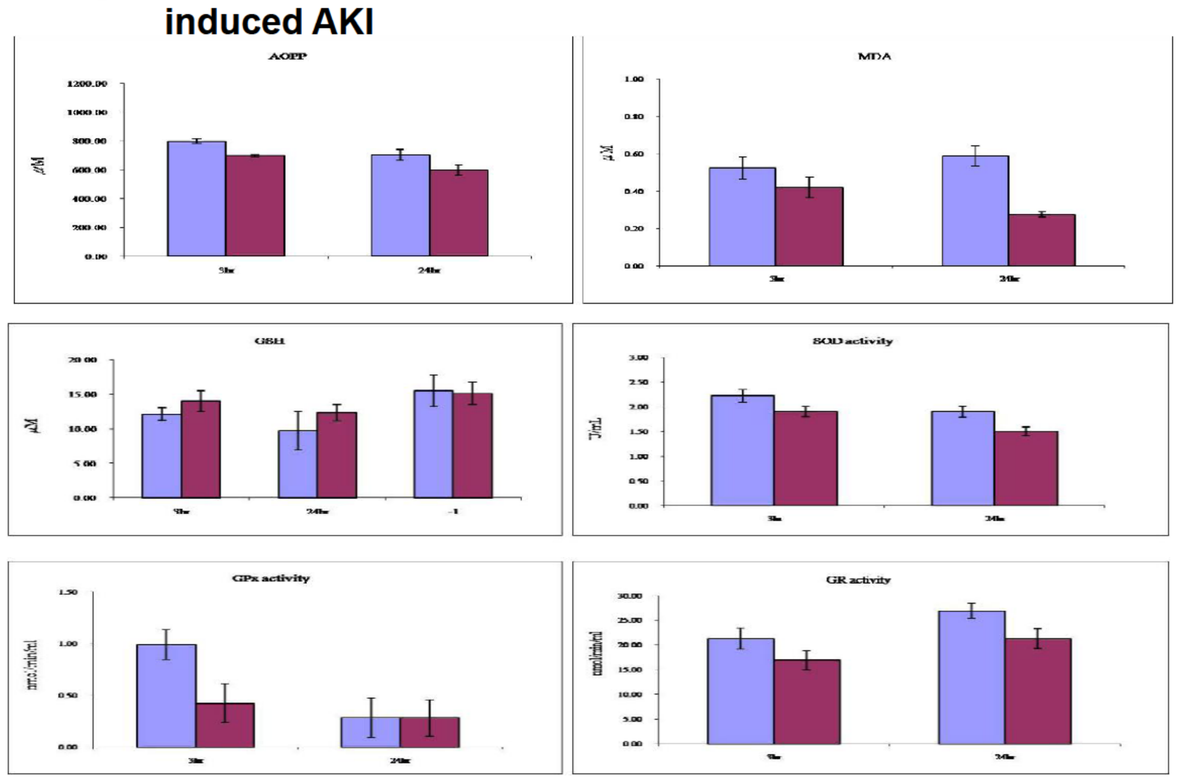
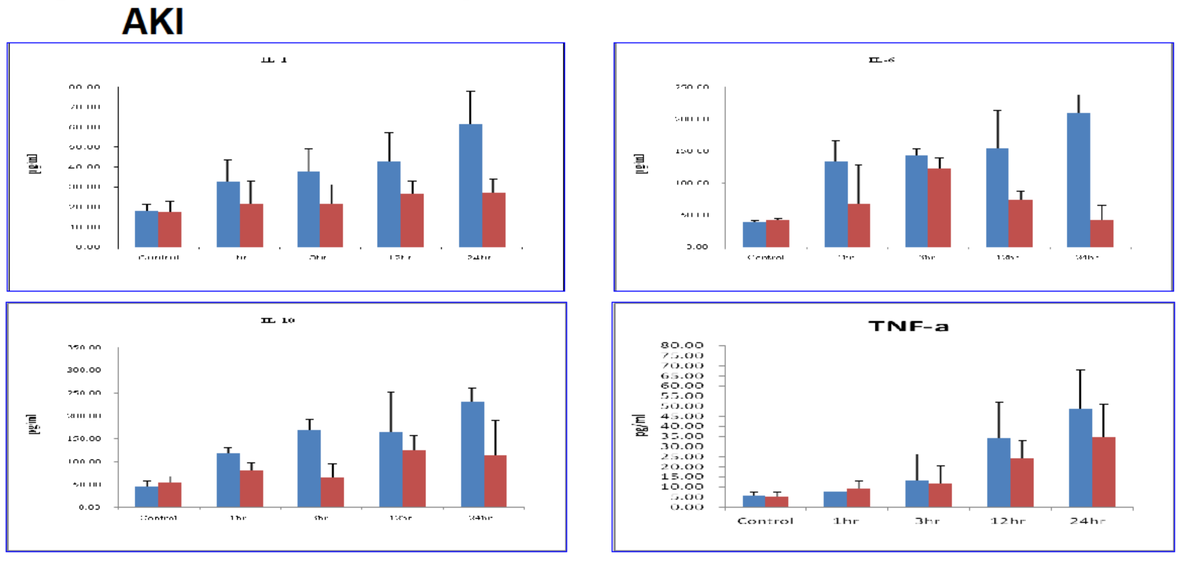


Fig. 6 Effects of NAC on cytokines in mice with HS induced AKI



Conclusion

Our studies have demonstrated NAC administration significantly attenuated organ damage and enhanced survival in HS rats. These protective effects may be associated with its anti-inflammatory capacity and anti-oxidant activity. Our study suggests that NAC could be potentially therapeutic for clinical HS induced AKI in the future.

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G) Acute Renal Failure. G1) Experimental models.

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