[SA171] N-ACETYLCYSTEINE IS AN APPROPRIATE THERAPY AT PREDETERMINING TIME OF ISCHEMIC ACUTE KIDNEY INJURY IN RATS

Mirian Watanabe,[1] Cassiane Fonseca,[1] Fernanda Borges,[2] Edson Pessoa,[2] Maria de Fatima Vattimo.[1]. [1]School of Nursing, Experimental Laboratory on Animal Models, University of Sao Paulo, Sao Paulo, SP, Brazil; [2]Nephrology Department, Federal University of Sao Paulo, Sao Paulo, SP, Brazil.

INTRODUCTION AND AIMS:
Severity of ischemia/reperfusion injury syndrome determines the prognosis of acute kidney injury (AKI). A number of processes have been implicated in the pathogenesis of oxygen deprivation induced cell injury. These include disturbance of generation of reactive oxygen species (ROS) with production of toxic lipid metabolites, and induction of protection mechanisms such as heme oxygenase-1 (HO-1) enzyme. HO-1 activity results in the removal of cell stressor and the production of biologically active metabolites by heme degradation with recognized antioxidant and anti-inflammatory action. N-acetylcysteine (NAC) is a small molecule containing a thiol group, which has antioxidant properties, promoting detoxification and acting directly as a free radical scavenger. This study evaluated the effect of NAC in protecting or restoring kidney function in a time dependent ischemic AKI animal model.
METHODS:
Adult, male, Wistar rats weighing 260 – 310 g were divided into following groups: SHAM (control), Ischemia 30 min (renal pedicles clamping for 30 min), Ischemia 30 + NAC (NAC 150mg/kg before and after 30 min renal ischemia), Ischemia 45 min (renal pedicles clamping for 45 min), Ischemia 45 + NAC. Renal function (creatinine clearance and urine sodium fractional excretion); oxidative injury (urinary peroxides, thiobarbituric acid reactive substances - TBARS, nitric oxide - NO and thiols in renal tissue); expression of HO-1 (western blotting) and kidney histological analysis (fractional interstitial area - FIA and tubuleinterstitial injury) were evaluated.
RESULTS:

[table1]

Groups (n)	Urinary Output (ml/min)	Creatinine Clearance / 100 g (ml/min)	Urinary Peroxides (nmol/g urinary cr)	TBARS (nmol/g urinary cr)	Urinary Nitrate (nmol/ g urinary cr)	Non-protein thiols (µmol/ mg protein)
SHAM (7)	0.011±0.001	0.97±0.02	1.7±0.1	56.7±7.2	30.2±2.2	170.2±15.8
Ischemia 30 (6)	0.031±0.001a	0.12±0.01a	5.9±0.2a	113.7±15.6a	76.6±6.6a	117.1±10.1a
Ischemia 30+NAC (6)	0.022±0.001a	0.57±0.08a	3.2±0.5b	58.1±6.7b	31.1±2.4b	89.4±4.0a
Ischemia 45 (6)	0.014±0.002b	0.04±0.01a	9.7±1.8ab	116.8±33.0a	76.2±14.5a	129.3±16.6b
Ischemia 45+NAC (6)	0.015±0.002b	0.02±0.01a	7.8±1.6a	117.1±13.4a	82.9±5.0a	103.7±9.0a

Results are reported as the mean±standard error. a $p<0.05$ vs SHAM; b $p<0.05$ vs Ischemia 30

Renal pedicles clamping for 45 min showed an increase in oxidative metabolites, loss of brush border, vacuolation of cells and acute tubule necrosis, with HO-1 expression. NAC was effective in reducing oxidative metabolites and tubuleinterstitial injury in the absence of HO-1 only in 30 min ischemic time.
CONCLUSIONS:
NAC intervention did not prevent redox disturbance and even worsened the 45 min ischemic AKI with expression of HO-1, an renal protective mediator. Our results do raise cautionary notes regarding the use of NAC, observing that, the more severe the AKI is, the higher levels of oxidative metabolites are. Also because auto-oxidation occurs during more pronounced situation of stress and it is involved with the severity of injury. It may explain why NAC was not effective in 45 min AKI.

Session: Moderated Poster Session: Acute Renal Failure - Experimental Models
Date/Time: Saturday, June 1, 2013 - 11:00 AM

Close Window