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REVERSE OF BLADDER OUTLET OBSTRUCTION ATTENUATE SYSTEMIC OXIDATIVE STRESS

Hypothesis / aims of study

As with benign prostatic hyperplasia (BPH), the prevalence of cardiovascular disease and diabetes appears to increase with age, which both are well known for increasing systemic oxidative stress. The first aim of this study is to investigate if partial bladder outlet obstruction (PBOO), a common complication from BPH, will increase systemic oxidative stress and if relief of PBOO will reverse the increasing systemic oxidative stress. Also, we will examine if urinary 8-OHdG, a popular biomarker, could be applied in this animal model. Moreover, we will explore the number of mitochondrial and level of 8-OHdG in bladder tissue.

Study design, materials and methods

We surgically created PBOO in male New Zealand White rabbits; after 4 weeks of PBOO, one group of four rabbits was assessed, while the PBOO was relieved in two additional groups of four rabbits each that were assessed at 4 and 8 weeks after relieving the PBOO. Four sham-operated rabbits served as controls. The oxidative stress biomarkers assessed included urinary and plasma 8-hydroxy-2′- deoxyguanosine (8-OHdG) and plasma malondialdehyde (MDA).We also measured the total antioxidant capacity (TAC) and glutathione (GSH) in blood plasma. 8-OHdG, MDA, TAC and GSH were measured at both the beginning and indicated time points of the experimental design. Copy number of mitochondria
and level of 8-OHdG of bladder tissue in each group were measured.

Results

Table. 1 The weights of bladder and rabbits

Mean (SD)	Group			
Variable	**C**	**O**	**R4**	**R8**
weight				
Rabbit (Kg)	3.96 (0.14)	3.4 (0.01)	3.6 (0.3)	3.6 (0.1)
Bladder (g)	2.21 (0.07)	18.75 (4.6) *	4.6 (1.11) ±	4.77 (1.16) ±

* significantly different from control, $P < 0.05$, ± significantly different from O 4 weeks, $P < 0.05$; t-test

Fig. 1 The biomarkers expressions of rabbits in Plasma

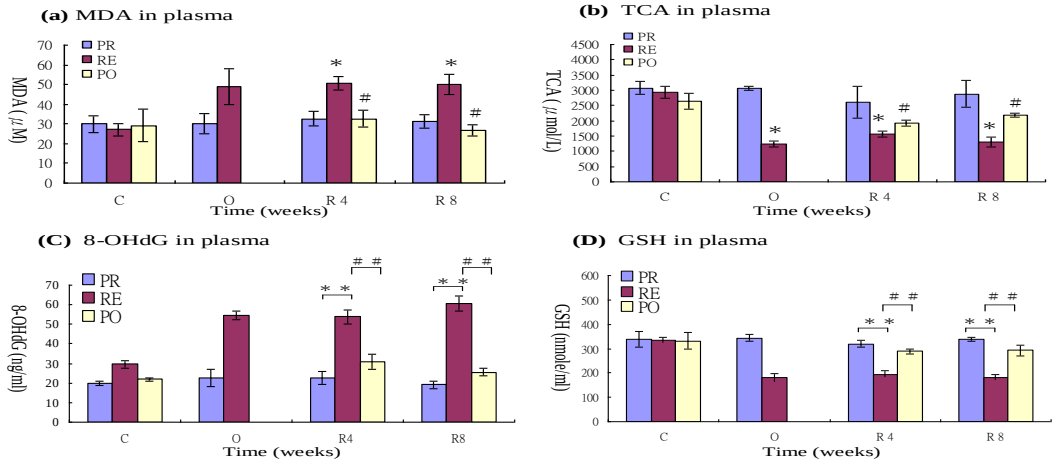
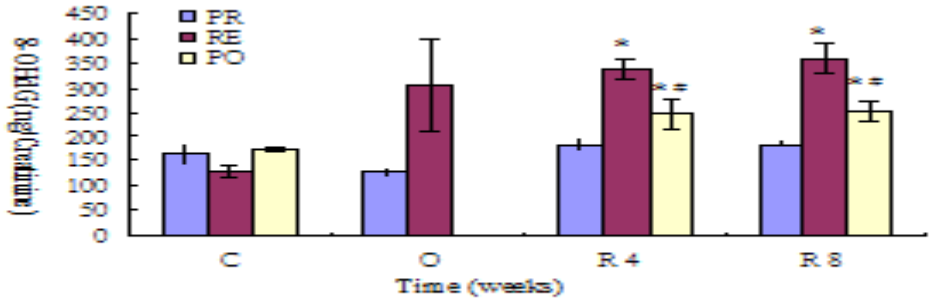


Fig. 2 The levels of 8-OHdG in Urine



PR: pre-obstruction, RE: post-obstruction, PO: reverse-obstruction
* significantly different from PR, $P < 0.05$,
# significantly different from RE, $P < 0.05$: *t* -test

Interpretation of results

There were significant increases in 8-OHdG (urine and plasma) and MDA (plasma) after PBOO and returned to control level after reversal of PBOO by 4 and 8 weeks. On the other hand, there were significant decreases in TCA (plasma) and GSH level (plasma) after PBOO and returned to control level after reversal of PBOO by 4 and 8 weeks. Also, there was significant decrease of the mitochondria DNA copy numbers in bladder tissues after PBOO and progressively returned to control level after reversal of PBOO by 8 weeks. Consistently, there was significantly increase in 8-OHdG level in bladder tissue after PBOO and progressively returned to control level after reversal of PBOO by 8 weeks .

Concluding message

PBOO will increase systemic oxidative stress, reflecting in plasma biomarkers of oxidative damage and antioxidant capacity. Reverse of PBOO will decrease systemic oxidative stress. Urinary 8-OHdG revealed parallel change with plasma biomarker of oxidative damage in PBOO and reverse of PBOO, which could be a more easy way for detection of bladder dysfunction. The mitochondrial number and level of 8-OHdG in bladder tissue also disclose the status of bladder function after PBOO or reverse of PBOO.

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Is this a clinical trial?	**No**
What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**The Animal Ethics Committee of Chang Gung Medical Foundation**