

Author(s) Alex T.L. Lin, K.K. Chen, Chin-Hua Yang and Luke S. Chang
Institution, city, country Division of Urology, Taipei Veterans General Hospital and Department of Urology, National Yang Ming University, Taipei, Taiwan
Title (type in CAPITAL LETTERS, leave one blank line before the text) OXIDATIVE DAMAGE ON RABBIT DETRUSOR MITOCHONDRIA FOLLOWING PARTIAL BLADDER OUTLET OBSTRUCTION
<u>Aims of study:</u> Experimental bladder outlet obstruction has shown to impair detrusor mitochondrial function with a decrease in energy production, resulting in contractile dysfunction. One possible cause for mitochondrial dysfunction is reactive oxygen species (ROS)-induced damages. We investigated oxidative effects on lipid and DNA of detrusor mitochondria, and determined mitochondrial superoxide dismutase (SOD) activity, a key ROS scavenger, following bladder outlet obstruction.
<u>Methods:</u> Bladder outlet obstruction was induced on male New Zealand rabbits. The bladders were removed 3(n=6), 7(n=6) and 14(n=6) days later. Sham operated animals served as the controls for each obstruction period. Detrusor mitochondrial SOD activity and mitochondrial content of malondialdehyde (MDA), a product of lipid peroxidation, and 8-hydroxydeoxyguanosine(8-OHDG), a biomarker of oxidative damage to DNA, were determined using high performance liquid chromatography(HPLC). Detrusor content of adenine nucleotides (ATP, ADP, AMP) was assayed and energy charge calculated according to the formula: $([ATP]+1/2[ADP]) / ([ATP]+[ADP]+[AMP])$. Energy charge represents energetic status of the tissue
<u>Results:</u> (1) Detrusor energy charge decreased in all obstruction groups. (2) Detrusor mitochondrial SOD activity persistently elevated following the obstruction (7.5, 6.4, 7.5 vs. 5.4, 4.2, 4.3 units/mg protein respectively for 3-, 7- and 14-days group), indicating a continually increased ROS generation. (3)MDA level increased in 3-days obstruction animals, and returned to control level in 7- and 14-days obstruction groups. (4) Detrusor mitochondrial 8-OHDG levels did not change in all obstruction animals.
<u>Conclusions:</u> Persistently elevated SOD activity and the enhanced lipid peroxidation activity during early obstruction period indicate an increase in ROS generation immediately following bladder outlet obstruction. ROS spare mitochondrial DNA, but peroxidize mitochondrial membrane lipid, resulting in mitochondrial damages, which may sustain and contribute to continually depressed energy producing ability and impaired contractile function.