

## EFFECT OF ALPHA-LIPOIC ACID ON REDUCTION AND OXIDATION PROCESS OF BLADDER IN A DIABETIC ANIMAL MODEL

### Hypothesis / aims of study

In addition to nephropathy and retinopathy, micturition disorders have been well recognized as a complication of diabetes. Recently, oxidative stress has been proposed as one of the major pathogenesis of complication in diabetes. Increased production of oxygen free radicals with diabetes could change in level of cellular reduction and oxidation and nitric oxide-mediated smooth muscle relaxation. The purpose of this study was to evaluate whether  $\alpha$ -lipoic acid, a potent antioxidant, affect pathologic reduction and oxidation process of bladder which resulted in voiding dysfunction in diabetic animal model.

### Study design, materials and methods

Twenty four 10 week-old male Sprague-Dawley rats with body weight 200-230g were used. Diabetes was induced by an intraperitoneal injection of streptozotocin (Sigma Chemical Co. USA) at a dose of 60mg/kg. Blood samples were taken from tail vein for glucose determination. The experimental groups included control group (n=6), untreated diabetic group (n=6) and diabetic group treated with 50mg/kg/day or 100mg/kg/day  $\alpha$ -lipoic acid (n=12) (Bukwang Pharm. Co., LTD., Korea) intraperitoneally for 8 weeks after induction of diabetes. The parameters for determination of the antioxidative effects were 8-hydroxy-2-desoxyguanosine (8-OHdG), a marker of oxidized DNA damage, apurinic/aprimidinic endonuclease (APE)/redox factor-1 (Ref-1), neural nitric oxide synthase (nNOS), and endothelial nitric oxide synthase (eNOS) expression by immunohistochemical staining and Western blot analysis, and ultra-structural changes of bladder smooth muscle cell by electron microscope in a diabetic animal model.

### Results

Nuclear immunoreactivity of 8-OHdG was not or weakly seen in control and, lipoic acid treated group, but was increased in diabetic group. APE/Ref-1, nNOS, eNOS protein expression were increased in diabetic group and inhibited by  $\alpha$ - lipoic acid treatment compared to control group. In electron microscope, there were a lot of mitochondria and vesicles in smooth muscle cells in control and  $\alpha$ - lipoic acid treated groups. In diabetic group, intracellular vacuoles were examined on perinucleus and cytoplasm of bladder smooth muscle cells and there is a few mitochondria. Cytoplasmic processes were well-developed in control and  $\alpha$ - lipoic acid treated groups but, poorly developed in diabetic group.

### Interpretation of results

The data showed that diabetes enhanced APE/Ref-1, nNOS, eNOS protein synthesis in bladder compared to control, which mean increased oxidative stress, and  $\alpha$ - lipoic acid treatment in diabetic animal inhibited expression of APE/Ref-1, nNOS, eNOS in bladder, which mean reduced oxidative stress.

### Concluding message

This study has highlighted the beneficial effects of early treated  $\alpha$ - lipoic acid in reducing or preventing the damages caused by oxidative stress and show that  $\alpha$ - lipoic acid may go far toward diabetic cystopathy.