The Effect of Antioxidants on the Response of the Rabbit Urinary Bladder to in Vitro Ischemia/Rreperfusion: Effects on Fatty Acid Metabolism

Robert M. Levin
Albany College of Pharmacy, Albany, New York, USA

Aims of Study: It has become evident that oxidative stress is a major factor in several lower urinary tract dysfunctions in both males and females. The specific aim of these current studies was to evaluate the protective effects of two naturally occurring antioxidants, alpha-lipoic acid and coenzyme Q10 on the response to in-vitro ischemia/reperfusion of the rabbit urinary bladder. We measured the effects on free fatty acid (FFA) content, phospholipid (PL) content, malondialdehyde (MDA) levels, and phospholipase A_2 activity (PLA) of subcellular compart-ments. We chose to study in vitro ischemia/reperfusion because we wanted to avoid the significant structural changes that occur in models of partial outlet obstruction (males) and ovariectomy (in females).

Materials and Methods: Twenty New Zealand White male rabbits were separated into four groups of 5 rabbits each. The in vitro whole bladders from groups 1 and 2 received a 3 hour incubation under normal oxygenated physiological conditions. The bladders were stimulated by field stimulation at 1 and 3 hours. The bladders from groups 3 and 4 underwent 1 hour incubation time under normal oxygenated physiological conditions. After 1 hour, the bladders were stimulated with field stimulation. After a maximal pressure response was recorded, the stimulation was turned off and the bath medium changed to one equilibrated with 95% nitrogen, 5% oxygen without glucose (ischemic medium) and incubated for 1 hour with field stimulations occurring at 5 minute intervals during this time. At the end of this hour of ischemia with repetitive stimulation, the bath was changed to an oxygenated medium with glucose for a 1 hour reperfusion period after which the stimulation was repeated. The rabbits from groups 2 and 4 received a-Lipoic acid (10 mg/kg/day) + Coenzyme Q10 (3 mg/kg/day) by gavage for 4 weeks prior to the experiment. At the end of the experimental period, each bladder was opened longitudinally and the muscle and mucosa separated by blunt dissection, frozen under liquid nitrogen, and stored at -80°C for biochemical analyses. Each tissue was fractionated by differential centrifugation into nuclear, mitochondrial, synaptosomal and cytosol (supernatant) components. PL, FFA, MDA, and PLA were analyzed using standard biochemical techniques.

Results: Post-ischemic contractility only returned to 30% of control of the untreated group. However, post-ischemic contractility of the treated group returned to approximately 70% of control. PL loss in the muscle mitochondria and synaptosomes was prevented by antioxidant treatment, while the mucosal layer showed a significant drop in PL with antioxidants treatment. Administration of CoQ+LA significantly decreased MDA levels in both control and ischemic tissues in both the muscle and mucosal bladder layers, especially substantial in the microsomal and mitochondrial components. Treatment had variable effects on PLA_2 activity.

Conclusions: Treatment of bladder dysfunction with antioxidants daily can be beneficial in man to prevent or delay the onset of progressive loss of bladder function especially that due to ischemic damage (Oxidative stress) to mitochondrial and microsomal lipids. CoQ10+LA can provide similar protection of the bladder muscle and mucosa against lipid oxidative stress as they have been shown to protect against protein oxidative damage.

Clinical Challenges of Male Incontinence: Post-prostatectomy Incontinence

Kyu-Sung Lee
Department of Urology, Samsung Medical Center, Sungkyunkwan University, School of Medicine, Seoul, Korea

Introduction

Despite improvements in surgical technique designed to preserve the functional integrity of the urethral sphincteric mechanism, incontinence after radical prostatectomy still occurs in many patients. Most patients with post-prostatectomy incontinence (PPI) have stress urinary incontinence (SUI) secondary to intrinsic sphincter deficiency (ISD). Patients with bladder dysfunction should be diagnosed and treated prior to surgical intervention.

Management of Post-prostatectomy Incontinence

The primary management of sphincteric incompetence after radical prostatectomy is bulking agents, artificial urinary sphincter and bulbourethral sling procedures. While pelvic floor exercise training and therapy instituted prior to radical prostatectomy aids in the earlier achievement of urinary incontinence, the value of the various approaches to conservative management of PPI generally remains uncertain (J Urol 2003; 170:130).

Since its introduction in 1993, bovine glutaraldehyde cross-linked collagen (Contigen; CR Bard, Covington, GA) has been used extensively as a bulking agent in the treatment of ISD in men. However, enthusiasm for this endoscopic procedure has waned because of the low success rates and the need for multiple treatments. In short-term studies, significant improvement or cure was achieved in approximately 20-62% of patients, but success rates declined dramatically with longer-term follow-up (J Endourol 1997; 11:273). Traditionally, collagen implant which is well tolerated and has low complication rate, has been recommended for mild to moderate incontinence in male SUI.

Various types of male sling procedures have been introduced over the years. Unlike the artificial urinary sphincter (AUS), the perineal male sling has the advantage of allowing spontaneous physiological voiding without need for manipulation. Bone anchored male sling appears to be effective and safe in intermediate term follow up. Excellent cure rates have been reported and they generally range between 70-90%

depending on the method of evaluation and definition of success (J Urol 2001; 165:72; J Urol 2002; 167:597; Eur Urol 2005; 47:237). Patient satisfaction rate of 70% with a mean follow-up of 24 months (Eur Urol 2005; 47:237). The sling failure correlated with the type of material and severity of the incontinence.

AUS is the gold standard treatment for PPI offering patients the greatest chance of cure. In the largest study to date, Elliott and Barrett reported 245 of 271 (90%) patients having a functioning AUS at mean follow-up of 5 years and 72% required no revision (J Urol 1998; 159: 1206). Another study with 61 patients and a 10-year follow-up reported a 75% continence rate, with 80% of patients having had at least one revision procedure by 10 years (Br J Urol 1997; 79:713). In spite of new technology, AUS continues to provide high patient satisfaction and cure rates.

Recently, various adjustable male slings have been introduced in Europe which can be adjusted according to patient needs and recurrence of urinary incontinence, such as ProACT (BJU Int 2005; 96:587), Reemix (J Endourol 2004; 18:113) and Argus (Arch Esp Urol 2006; 59: 607). Recently, Rehder and Gozzi reported the safety and efficacy of a transobturator sling suspension, which may offer further advantages, including the avoidance of bone anchors, but data on outcomes are still pending (Eur Urol 2007; 52:860).

Summary

Most patients with PPI have SUI secondary to ISD. Patients with bladder dysfunction should be diagnosed and treated prior to surgical intervention. The AUS is the gold standard in treating patients with stress incontinence. Collagen injection therapy plays a very limited role in the PPI patients. Various bulbourethral slings, especially bone-anchored male sling and new devices provide an alternative therapy to the AUS.