

## **NITRIC OXIDE DONOR URETHRAL PRESSURE PROFILOMETRY IN EVALUATION OF VOIDING DYSFUNCTION**

### **Aims of Study**

Among the various etiology of voiding dysfunction, neurogenic detrusor external sphincter dyssynergia (DESD), dysfunctional voiding due to spastic urethral sphincter, non-relaxing urethral sphincter and detrusor underactivity are the most commonly encountered pathology that result in difficult urination, large residual urine, and upper urinary tract deterioration. The therapeutic modalities for these diseases include transurethral sphincterotomy, alpha-blockers, skeletal muscle relaxants, and pelvic floor re-education. However, none has been demonstrated to have long-term therapeutic effect currently. Nitric oxide is an inhibitory neurotransmitter synthesised by nitric oxide synthase. Both animal and human studies suggest that nitric oxide mediates urethral sphincter relaxation. The rapid onset and short half-life of glyceryl trinitrate (nitroglycerine) is an ideal drug to assess the response of the urethral function. The purpose of this study is to investigate the urethral response to sublingual nitroglycerine in the patients with various etiologies of voiding dysfunction who were refractory to the above mentioned treatment.

### **Methods**

Fifty patients with dysuria or urinary retention of various etiologies who were refractory to conservative treatment underwent urethral pressure profilometry (UPP) by perfusion method. In addition, 10 patients with stress urinary incontinence (SUI) without voiding dysfunction served as comparative group. UPP study was performed with an 8 Fr dual-lumen catheter. The perfusion rate was 4 ml/min and the catheter withdrawal rate was 1 mm/s. All patients underwent three consecutive UPP studies at first. Then a 0.6 mg nitroglycerine was given sublingually. Another 3 consecutive UPP studies were performed 2 minutes after nitroglycerine treatment. The blood pressure was monitored at baseline and after nitroglycerine treatment. The maximal urethral closure pressure (MUCP) and functional profile length (FPL) were compared between baseline and post-treatment. Any adverse effect was recorded related to nitroglycerine treatment during investigation. Patients who had response to nitroglycerine were treated with isosorbide mononitrate (Corangin) and the therapeutic effect was evaluated.

### **Results**

The patients enrolled in this study included 10 patients with SUI and 10 patients each who had voiding dysfunction due to spastic urethral sphincter, after radical hysterectomy, spinal cord lesions, after prostatectomy, and frequency urgency syndrome. A more than 20% reduction in MUCP was found in 60% of the patients. No significant change was noted in FPL between baseline and post-treatment. According to the subgroup categories, the reduction of MUCP was more commonly found in patients after radical hysterectomy, followed by those with dysfunctional voiding and after prostatectomy. Patients with spinal cord lesions and DESD did not show significant reduction of MUCP. Interestingly, all patients with SUI had a significant reduction of MUCP whereas the patients with frequency urgency syndrome did not show significant reduction in MUCP after nitroglycerine treatment.

The therapeutic effect in the patients who had response to nitroglycerine was not remarkable in the patients with DESD or after prostatectomy. However, 70% of the patients with dysfunctional voiding and 60% of patients after radical hysterectomy had subjective improvement in voiding efficiency and obstructive symptom score. However, the maximal flow rate did not show significant increase after nitric oxide donor treatment.

### **Conclusions**

The results of this study demonstrate that glyceryl trinitrate can be used as a provocative test in UPP study. Supplement of exogenous nitric oxide causes relaxation of urethral sphincter muscles. In the patients with partial denervation after radical hysterectomy, the response is more remarkable. In the patients with SUI, the response to nitric oxide is far more remarkable, suggesting a weak striated muscle component might exist in these patients and relaxation of smooth muscle can result in a significant reduction of MUCP. For the patients who had DESD and spastic urethral sphincter, and for those with a potentially normal urethral sphincter muscles, MUCP were not reduced possibly because the abundant striated muscle component respond less to nitric oxide. Although reduction of MUCP was remarkable, voiding efficiency and maximal flow rate are not correlated well. This fact further reveals that micturition is a process more complex than simple reduction of urethral smooth muscle tone.

