

## Transurethral electrochemical treatment of benign prostatic hyperplasia

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**Objective** To study the mechanism and feasibility of transurethral electrochemical therapy for the treatment of benign prostatic hyperplasia (BPH).

**Methods** Between March 1998 and March 2000, specifically designed devices and catheters for electrochemical therapy were applied to 6 prostate specimens obtained by suprapubic prostatectomy in order to treat BPH patients with urinary retention for whom surgery was contraindicated. Sixteen patients (with a mean age of 77.3 years old) underwent electrical treatment totaling 160 – 220 coulombs under topical urethral anesthesia for 68 – 132 min. The catheters remained inside the patient for 7 – 10 d.

**Results** Irreversible destructive changes occurred within cathodal tissue, while carbonization occurred within anodic tissue. The radius of tissue change was 7 – 8 mm and 1 – 2 mm, respectively. *In vivo* trial: 11 (69%) patients could be weaned off the catheters with satisfactory urination. Three months after therapy, the mean international prostate symptom score (IPSS) was 14.5, mean peak flow rate was 10.5 ml/s, and mean residual urine was 39 ml. No serious complications were observed.

**Conclusion** Transurethral electrochemical treatment is potentially a minimally invasive alternative for treatment of BPH, especially for elderly patients at high risk.

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Electrochemical treatment has achieved success as an anticancer therapy through the insertion of platinum electrodes into the tumor which are then connected to a direct current. Strong alkalinity and acidity at the cathode and anode respectively, as well as free chlorine, oxygen and hydrogen produced as a result of electrolysis can destroy tumor cells.<sup>1-5</sup> We studied the feasibility of transurethral electrochemical therapy as a treatment for benign prostatic hyperplasia (BPH) by causing necrosis of prostatic tissue within the target zone.

### METHODS

Between March 1998 and March 2000, we used the EASY-100A electrochemical therapeutic instrument for BPH (Exland Medical Instruments Technology Co. Ltd., Tianjin, China) on six prostate specimens obtained by suprapubic prostatectomy. The instrument was also used on 16 BPH patients who had urinary retention, for whom surgery was thought to be contraindicated.

### Apparatus

The therapeutic instrument is a direct current generator that is adjustable for current between 6 – 99.9 mA, for electrical

quantity between 50 – 9999 coulombs and a rising slope of current between 0.2 – 9.99 mA/s. The amount of 120 – 160 coulombs was recommended for patients with prostate hyperplasia grade I, 170 – 210 coulombs for grade II and 220 – 250 coulombs for grade III. The recommended rising slope of current was 0.2 mA/s. The therapeutic catheter is an 18F balloon-type urological catheter with flexible platinum cathodes and anodes twined alternately on the surface of the catheter with an interval of 0.5 cm. The electrodes can be suitably placed in the prostatic urethra using the balloon. Ideally, the total length of electrodes is 0.5 – 1.0 cm shorter than that of prostatic urethra.

### *In vitro* study

Six prostate specimens were obtained by suprapubic prostatectomy. The mean weight was 81 g (ranged from 42 to 158 g). Upon removal, the prostate specimens were immediately dipped into 0.9% saline. Suitable therapeutic catheters, which were selected according to the length of

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prostatic urethra, were placed in the prostatic urethra. Different levels of electricity were set, 120 – 160 coulombs for 2 prostate specimens, 170 – 210 coulombs for 2, and 220 – 250 coulombs for 2. The temperature of prostates was monitored continuously by an intercalary electronic thermometer during the therapeutic procedure. The prostate specimens were incised lengthwise first, and then transversely after the therapy to examine their appearances and the longitudinal length and depth of the affected tissue. After gross examination and measurement, the specimens were fixed in 10% neutral formalin solution for at least 24 h. Slices were cut vertically every 0.5 cm from the apex to the base of the prostate along the axis of the prostatic urethra. Routine paraffin processing was applied. Ten to twenty sections were obtained from each prostate. Specimens were stained with hematoxylin-eosin (HE) for histological study.

#### *In vivo* trial

A total of 16 BPH patients with urinary retention whose cases were deemed inoperable were enrolled in this study. The mean age of patients was 77.3 y (ranged from 71 to 93 y). Of them, 10 patients were complicated by coronary heart disease, 4 had chronic bronchitis, 2 had cerebral vascular diseases, 5 had other diseases, and 2 refused surgery. Prostatic volume was measured by transrectal ultrasonography according to the following formula: prostatic volume = prostate height × prostate width × prostate length × 0.523. The mean prostatic volume was  $69.5 \pm 24.6$  ml. Fourteen patients had indwelling urethral catheters. Two patients had been required to undergo suprapubic cystostomy. The length of prostatic urethra was determined accurately either by transrectal ultrasonography or by endoscopy to select suitable therapeutic catheters. Indwelling catheters were retained for a mean period of 2.1 months (ranged from 0.5 to 4.0 months).

After urethral lubrication with 2% lidocaine jelly, the therapeutic catheter was inserted and the electrodes positioned in the prostatic urethra by withdrawing the inflated balloon catheter. The electrodes were then connected to the EASY-100A electrochemical therapeutic instrument. Electricity was set at 160 – 220 coulombs. The instrument increased the amount of electricity automatically and stopped at the set value. Treatment was administered for 68 – 132 min. The therapeutic catheter was withdrawn, after treatment, and another Foley catheter was put in place. Oral antibiotics were administered for 3 – 5 d.

Patients remained catheterized for 7 – 10 d. Post-treatment follow-up was performed after the catheters were withdrawn, one month and three months after treatment. Follow-up included assessment of urinary performance, international

prostate symptom score (IPSS), uroflowmetry with maximal flow nomogram, determination of residual urine volume by catheter, and determination of prostatic volume by transrectal ultrasonography. A proportion of the patients underwent urethroscopy before treatment after the catheters were withdrawn and 1 month after treatment.

## RESULTS

#### *In vitro* study

The temperature of prostate was stable during the therapeutic procedure. The prostate specimens were incised lengthwise and a fawn alternating black surface was observed along the urethra. A fawn colloidal surface was placed around every cathode, while a black carbonized surface surrounded every anode. The total length of changed tissue was 5 – 8 mm longer than that of the selected cathode. On transverse sections, cathodal colloidal change occurred within a radius of 6 – 9 mm from the surface of the urethra, while anodic carbonization occurred within a radius of 1 – 2 mm. Changes in urethral tissue were symmetrical at all radii. The lengths and depths of tissue changes did not show any significant differences among groups treated with different levels of electricity.

Under the microscope, three zones were identified in cathodal tissue from the surface of the prostate urethra to the surgical capsule of the prostate. There was a necrotic zone around the prostate urethra, 1 – 2 mm in depth. The normal structures of urethral mucosa and adjacent tissue were replaced by necrotic materials. A degenerative zone, 4 – 6 mm in depth, was located outside the necrotic zone. The nuclei of gland cells were enlarged and showed enlarged nucleoli and degenerated cytoplasm. Degeneration was also observed in periglandular stroma. Beyond the degenerative zone was a normal zone where no significant changes were observed. A clear border existed between the degenerative zone and the normal zone. There was no relationship between the depth of histological change and the levels of electricity. Nevertheless, the greater the electricity used, the more severe necrosis and degeneration were detected. Around anodes, there were few carbonized materials without cellular structures. It was presumed that more carbonized materials had fallen off while the slices were being made.

#### *In vivo* trial

All of 16 BPH patients completed the therapeutic procedures. Mean therapeutic time was 82 min (ranged from 68 to 132 min). Of the 16 patients who presented with urinary retention, 13 regained spontaneous voiding shortly after the catheters were withdrawn 7 – 10 d post-treatment. Three patients remained catheterized permanently because of an inability to urinate spontaneously. Of the 13 patients who

regained spontaneous voiding, two patients were recatheterized within one month after treatment because of severe obstructive symptoms or a large residual urine volume (> 100 ml). By three months after treatment, clinically significant improvements were noted, including the following: 11 (69%) patients were weaned off the catheters with satisfactory urination, a mean IPSS of 12.5, a mean peak flow rate of 10.5 ml/sec, and a mean residual urine volume of 39 ml. Prostatic volumes measured before treatment and one month after treatment were  $69.5 \pm 24.6$  ml and  $68.7 \pm 28.5$  ml, respectively ( $P > 0.05$ ). Urethroscopy performed within 7 - 10 d after treatment showed necrosis and exfoliation of prostatic urethra mucosa. By one month after treatment, a thickened prostatic urethra covered with normal mucosa was observed.

Mild toxicity was observed in our study. Involuntary bladder spasm was the most common side effect during therapeutic procedure, manifesting as slight suprapubic discomfort. Hematuria was mild and temporary, required no treatment and ceased within 1 - 2 d. There were no serious complications such as severe hematuria, urinary tract infection, or incontinence.

### DISCUSSION

Experimental and clinical studies on electrochemical therapy have a long history.<sup>6</sup> In 1895, Golsinger inserted electrodes into canine brains, stimulated them with 20 - 40 mA of direct current and observed that degeneration and necrosis occurred in cerebral tissue around electrodes. In 1983, Nordenströme reported electrochemical treatment for lung cancer patients. In China, nearly 6000 patients with various kinds of neoplasms underwent electrochemical treatment.<sup>7</sup> Electrochemical treatment is based on Nordenströme's hypothesis of the vascular-interstitial closed-circuit system (VICC).<sup>8-11</sup> The VICC, existing between the blood plasma and the extravascular tissue fluid to provide circulation of energy, can be activated artificially by an electric current between electrodes implanted in tissue, e.g., between cancer and surrounding normal tissue. Electrophoresis starts with the transport of negative ions to electropositive electrodes and positive ions to the electronegative electrodes. The following changes may occur: The decomposition of water at the anode results in strong acidity with pH values falling to 1 - 2, while alkalinity occurs at the cathode with the pH values rising to 11 - 13. Free oxygen and chlorine form at the anode, and hydrogen evolves at the cathode. Electroosmosis affects the water content of tissue, resulting in edema of cathodal tissue and dehydration of anodic tissue. Electrophoresis may induce local accumulation of leukocytes and thrombocytes. Thus, the environment around the cancer cells can be considerably

altered and neoplasms under these conditions may regress selectively. It should be emphasized that the electrochemical effect is different from that of hyperthermia and thermotherapy. Because the human body is resistant when electrified with direct recurrent, the temperature of 2000 ml of tissue rises by mere 0.285 °C, and blood and lymph can absorb that quantity of heat.

Transurethral resection of the prostate and open prostatectomy are still the most common surgical procedures performed in elderly BPH patients. Nevertheless, the indication, risks, and benefits have recently been under scrutiny. Although they are generally perceived as being effective procedures, the associated morbidity, mortality, and rate of failure have prompted searches for alternative therapeutic modalities, both medical and device-related. Inspired by electrochemical therapy for tumors, we attempted to adapt transurethral treatment for BPH patients. Our *in vitro* study showed that electrochemical therapy caused irreversible destructive changes within proliferated prostate tissue. In our *in vivo* study, all 16 BPH patients tolerated the therapeutic procedure. Except for temporary hematuria, the complications associated with the therapy were minimal and rare. A total of 11 (69%) patients could urinate spontaneously after the catheters were removed. The safety and effectiveness of transurethral electrochemical therapy has been demonstrated.

Accurate determination of the length of prostatic urethra and suitable selection of therapeutic catheters is very important for increasing effectiveness and reducing complications. Through urethroscopy, we found that necrosis and exfoliation was mild in the proximal or distal part of prostatic urethra among the patients with dissatisfied outcomes, suggesting that the electrodes on the selected catheters were too short. Excessively long cathodes, however, would increase the risk of incontinence.

In summary, we believe that transurethral electrochemical therapy, as a minimally invasive treatment, should be available for BPH patients with urinary outflow obstruction who are poor operative risks. This treatment is easy to administer on an outpatient basis, is well tolerated by patients under topical urethral anesthesia alone, and results in minimal change of local temperature and mild toxicity. More treatment data and longer follow-up are necessary for further evaluation of this treatment modality in BPH patients.

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