Results of a 5-Year Multicenter Trial of a New Generation Cooled High Energy Transurethral Microwave Thermal Therapy Catheter for Benign Prostatic Hyperplasia

Lance A. Mynderse,* Claus G. Roehrborn,† Alan W. Partin, Glenn M. Preminger‡ and Eric P. Coté

From the Departments of Urology, Mayo Clinic (LAM), Rochester, Minnesota, and University of Texas Southwestern (CGR), Dallas, Texas, Urology Department, The Johns Hopkins University Hospital (AWP), Baltimore, Maryland, Department of Surgery/Urology, Duke University Medical Center (GMP), Durham, North Carolina, and Virginia Urology Center (EPC), Richmond, Virginia

Abbreviations and Acronyms

AUASS = American Urological Association symptom score

BII = BPH Impact Index

BPH = benign prostatic hyperplasia

CTC = cooled ThermoCath standard microwave catheter

MRI = magnetic resonance imaging

PSA = prostate specific antigen

PVR = post-void residual urine

Qmax = maximum flow rate

QOL = quality of life questionnaire

SAE = serious adverse event

SPI = Symptom Problem Index

TRUS = transrectal ultrasound

TUMT = transurethral microwave thermal therapy

TURP = transurethral prostate resection

VAS = visual analog scale

Submitted for publication October 11, 2010.

Study received institutional review board approval.

* Financial interest and/or other relationship with Urologix, PNN Medical and AMD Medical.

† Financial interest and/or other relationship with Urologix.

‡ Financial interest and/or other relationship with Mission Pharmacal and Boston Scientific.

Purpose: We determined the safety, effectiveness and 5-year durability of the new generation, cooled, high energy microwave treatment Cooled ThermoCath® catheter with the Targis® cooled high energy transurethral microwave thermal therapy system by performing a prospective, multicenter trial in men with lower urinary tract symptoms and clinical benign prostatic hyperplasia.

Materials and Methods: At 5 American centers a total of 66 men were treated with the catheter at a 28.5-minute session. Patients were taught self-catheterization after treatment. They returned after 1 and 6 weeks, 3 and 6 months, and annually for 5 years to assess the American Urological Association symptom score, uroflowmetry, quality of life, Symptom Problem Index, Benign Prostatic Hyperplasia Impact Index, treatment satisfaction, adverse events and need for re-treatment.

Results: Average treatment duration was 29 minutes. Of the 66 men 33 (50%) required no posttreatment catheterization of any kind, 25 (38%) used intermittent self-catheterization and 8 (12%) required indwelling catheterization with or without self-catheterization. No acute retention events were reported after the initial catheterization through 5 years. No serious adverse events were associated with treatment. Traditional efficacy measures showed highly significant improvement from 6 weeks and thereafter ($p < 0.001$). A total of 19 men (29%) underwent additional medical or surgical benign prostatic hyperplasia related treatment at some time during the 5-year followup. Six men (9%) underwent surgical benign prostatic hyperplasia related treatment. At 5 years 40 of 51 men (78%) reported satisfaction with benign prostatic hyperplasia treatment.

Conclusions: Cooled, high energy transurethral microwave thermal therapy using a new generation treatment catheter produced safe, durable, clinically relevant results in men with lower urinary tract symptoms caused by benign prostatic hyperplasia for 5 years after treatment with acceptable medical and surgical re-treatment rates.

Key Words: prostate; prostatic hyperplasia; microwaves; hyperthermia, induced; catheterization

MICROWAVE therapy for male lower urinary tract symptoms and clinical BPH has evolved considerably in the last 30 years. In the 1980s investigators used lower powered microwave treatments, which generated a small depth of penetration and were referred to as hyperthermia.[1] Through

0022-5347/11/1855-1804/0
THE JOURNAL OF UROLOGY®

Vol. 185, 1804-1810, May 2011
Printed in U.S.A.
DOI:10.1016/j.juro.2010.12.054

the 1990s most of these treatments were phased out due to side effects and lack of efficacy. Higher powered systems with rudimentary cooling systems were designed to allow deeper penetration of heat into the prostate at higher temperatures while protecting the urethral lining and preventing pain perception. In 1996 the first transurethral microwave thermotherapy device was approved in the United States.[2]

Today TUMT can be divided into 2 distinct types, that is high and low high energy. Only TUMT devices with greater than 50 W of power show significant improvement in obstruction.[3–7] Djavan et al compared cooled high energy TUMT to α-blockade and noted its superiority in the magnitude and durability of effectiveness for TUMT.[8] High energy TUMT devices are designed to decrease treatment time and improve patient comfort.[9]

We present clinical outcomes in a cohort of patients treated with a new generation, cooled, high energy microwave treatment catheter that demonstrate its safety, efficacy, tolerability and durability at a shorter treatment session.

METHODS AND MATERIALS

Study Design

This was a single arm, prospective, multicenter study of new generation, high energy microwave treatment for BPH using a CTC compared to the previous Targis cooled TUMT system. We evaluated the safety and efficacy of 28.5-minute CTC TUMT in noninferiority comparisons using previously approved, 60-minute cooled TUMT system treatment.[3,10] The study was designed to enroll up to 110 patients but enrollment was halted due to a slower than projected enrollment rate. This investigational device exemption study was performed under institutional review board oversight.

Patient Requirements

Patients were identified from existing practices or recruited from the local population. All patients provided written informed consent before screening. Patients were 45 to 85 years old and had an AUASS of 8 or greater, Qmax 15 ml per second or less, prostatic urethral length 30 to 50 mm, PSA less than 8 ng/ml or negative prostate biopsy. Patients underwent a 30-day washout for antiandrogens or α-blockers, and a 60-day washout for 5-α reductase inhibitors. Patients were excluded from study if they had PVR greater than 300 ml, prostatitis, neurogenic bladder and/or sphincter abnormalities, urinary retention requiring catheterization within 6 months of study enrollment, urethral stricture, asymmetrical median lobe enlargement or a prominent obstructing ball valve prostatic lobe, required fertility preservation, had evidence of prostatic or bladder cancer, or prostate weight greater than 100 gm, or underwent a prior procedure for BPH.

Study Performance

Baseline evaluation included medical history and digital rectal examination. Symptoms were assessed with AUASS and a QOL question,[11,12] SPI, BII[13] and additional questions on satisfaction with treatment. Uroflowmetry, cystoscopy and TRUS were done. Laboratory tests included creatinine, PSA, urinalysis and urine culture.

Followup assessments included symptom questionnaires, and PSA, creatinine, uroflowmetry and adverse event assessment. Followup visits were performed at 1 and 6 weeks, 3, 6 and 12 months, and yearly thereafter through 5 years after treatment. TRUS and cystoscopy were done at month 6. In a subset of patients gadolinium enhanced MRI was completed 1 week after treatment to examine necrosis using the methods of Osman[14] and Huidobro[15] et al.

Treatment was performed on an outpatient basis with preemptive analgesia and/or anxiolytics administered before treatment. Before inserting the treatment catheter lidocaine viscous gel, lidocaine/bupivacaine solution and antispasmodic medications were administered. No medications were administered intravenously and neither regional nor general anesthesia was used. Before, during and after treatment pain intensity was measured with a VAS. After treatment patients were administered nonsteroidal anti-inflammatory drugs and antibiotics. At hospital discharge patients were provided instructions and materials for self-intermittent catheterization.

Statistical Analysis

The study objective was to rule out the inferiority of the new CTC 28.5-minute TUMT compared to the previously approved 60-minute treatment.[3,10] One-sided statistical tests were used for primary safety and efficacy analyses.

The Qmax rates used were those sustained for 2 seconds or greater. Qmax values were excluded from analysis if the patient voided less than 125 ml. Changes from baseline Qmax, AUASS and QOL were determined using the paired t test to determine whether the change differed significantly from zero. Hypothesis tests were confirmed using intent to treat analysis for CTC treatment only. Efficacy measures were analyzed by intent to treat analysis using the last value carried forward for missing data.

Re-treatment was defined as any BPH medication for greater than 2 weeks at 90 days or greater after treatment or any surgical treatment, eg surgical procedures such as laser therapy or TURP. Kaplan-Meier analysis provided estimated re-treatment rates adjusted for censored patients. Patients were censored at study completion, early withdrawal due to loss to followup or diagnosis of a confounding medical condition, eg prostate cancer. The association between the re-treatment outcome and select baseline covariates was assessed using Cox proportional hazards regression. The statistical software used was SAS®, version 9.1 or higher.

RESULTS

Screening and Baseline Characteristics

Of 162 screened patients 70 met selection criteria and were enrolled in the study between February 28, 2002 and March 2, 2004. A total of 66 patients