WATER-INDUCED THERMOTHERAPY OF BENIGN PROSTATIC HYPERPLASIA

ISSUE

Blue Shield continues to receive requests for coverage of transurethral water-induced thermotherapy for symptoms of urinary obstruction due to benign prostatic hyperplasia. The Medical Policy Committee on Quality and Technology is asked to evaluate this new technology.

CURRENT BLUE SHIELD POLICY

On June 18\textsuperscript{th} 1997, the Medical Policy Committee on a consent calendar item adopted the national Blue Cross Blue Shield Association policy on transurethral microwave thermotherapy of the prostate. On June 10\textsuperscript{th} 1998, the Medical Policy Committee approved transurethral needle ablation of the prostate. Both of these procedures are eligible for coverage as medically necessary for patients with symptoms of urinary obstruction due to benign prostatic hyperplasia. In addition, transurethral resection of the prostate (TURP) and open prostatectomy are eligible for coverage.

BACKGROUND

Benign prostatic hyperplasia is the most common benign tumor in men. Symptoms of prostatic obstruction are age-related. At age 55, approximately 25\% of men report obstructive voiding symptoms, and at age 75 years, 50\% of men report a decrease in the force and caliber of the urinary stream (Stoller et al, 2001).

Many men with benign prostatic hyperplasia (BPH) respond to medical therapy with alpha-adrenergic receptor blockers such as terazosin (Hytrin) or 5-alpha-reductase inhibitors such as finasteride (Proscar). However, in the U.S., approximately 20\% of men eventually require an operation to relieve symptoms due to BPH (Arrighi et al, 1990). Transurethral resection of the prostate (TURP) or an open prostatectomy are currently available as surgical options for symptomatic patients with BPH. Almost all patients who elect to have surgery undergo TURP and find it satisfactory in its effectiveness with minimal mortality. However, at least 15-20\% of patients undergoing TURP will develop a significant complication (e.g., incontinence, urethral stricture, or hemorrhage necessitating transfusion) and between 10\% and 15\% of cases will need a second intervention within 10 years (Roos et al, 1989; Mebust et al, 1989).
BACKGROUND, continued

Recently, various thermal therapies have been investigated as less invasive surgical procedures for BPH, including transurethral microwave thermotherapy, transurethral needle ablation of the prostate (TUNA), high intensity focused ultrasound therapy, and laser delivered interstitial thermal therapy. These procedures use different forms of energy, such as microwave, ultrasound, laser, and radiofrequency to produce the thermal injury, which in turn leads to either anatomical shrinkage or debulking of the obstructing enlarged prostate or physiological alteration of voiding function (Issa, 1996).

Transurethral Water-induced Thermotherapy (WIT)

Transurethral water-induced thermotherapy (WIT) is a catheter-based, “minimally invasive” treatment that involves an extracorporeal heat source and a closed loop balloon catheter system. The technique involves circulation of hot water (60°C) through a dilated catheter balloon placed transurethally into the prostatic urethra. The combination of heat and compression by the balloon causes thermal energy to be conducted to the targeted prostatic tissue (Cioanta et al, 2000). The catheter also includes thermal insulation to protect nontargeted tissues such as the internal urinary sphincter and the rectum (Muschter et al, 2000). Treatment balloons are available in various lengths from 2.0 to 6.0 cm, in 5-mm increments, to match the length of the prostatic urethra in the individual patient.

The mechanism of action of WIT is thought to involve coagulative necrosis of prostatic tissue. Significant post-treatment shrinkage of the prostate gland has been noted (Muschter et al, 2000).

WIT offers several potential advantages. First, it can be rapidly performed. The WIT procedure requires approximately 45 minutes. Second, it can be performed in the outpatient setting with only intraurethral analgesia and intravenous sedation; general anesthesia is unnecessary. Third, the thermal ablation is well-localized and can be accurately controlled by the length of the catheter’s balloon and thermal insulation used, thus protecting and preserving adjacent structures, such as the urinary sphincter and rectum. Finally, WIT is “minimally invasive,” convenient, and does not require special facilities.
TA Criterion 1

In 1999, the Thermoflex Water-Induced Thermotherapy System™ (ArgoMed, Inc., Cary, North Carolina) received FDA approval through a 510(k) for the following indication: “The Thermoflex system is intended for the treatment of symptoms due to urinary outflow obstruction secondary to benign prostatic hyperplasia (BPH). It is indicated for use in men over the age of 50 years with prostate lengths between 2.0 cm and 6.4 cm who present with symptoms of urinary outflow obstruction secondary to BPH.”

TA criterion 1 is met.

TA Criterion 2

No randomized controlled trial examining the efficacy and safety of WIT has been published.

There has been a single prospective, uncontrolled, multicenter clinical study of WIT for BPH (Muschter et al, 2000). An abstract providing 2 year follow-up of the subjects in this trial and one providing 3 year follow-up (Muschter et al, 2001) have been published. (Schorsch et al, 2000; Muschter et al, 2000). This trial did not compare WIT to other methods of treatment, such as TURP or TUNA or transurethral microwave thermotherapy of the prostate a third abstract (Brasi et al, 2001) has reported on use of WIT for patients with BPH and urinary retention.

The single published study included men over age and 50 with chronic symptoms of BPH and International Prostate Symptom Score (IPSS) of ≥ 13, and peak urinary flow rates <12 mL/sec with a voided volume 125 mL based on a minimum of two uroflow measurements. The study excluded men if they had carcinoma of the prostate; previous prostatic, radical pelvic, or rectal surgery or radiation, prostate specific antigen > 10 ng/mL; bladder stone or hematuria; median prostate lobe protruding into the bladder; history of urethral strictures, bladder neck contracture, or bladder pathology; active urinary tract infection, urinary retention, or immunosuppression; neurogenic bladder and and/or sphincter abnormalities; use of medications that might interfere with voiding, post-void residual > 250 mL, or renal insufficiency with serum creatinine > 1.8 mg/dL (Muschter et al, 2000).
TA Criterion 2, continued

Evaluations of the clinical effects of WIT included International Prostate Symptom Scores (I-PSS); mean and peak urinary flow rates on uroflowmetry; post-void residual urine volumes; quality of life scale scores; sexual function questionnaires; and immediate complications.

With only one uncontrolled study of WIT, published data are insufficient to assess its safety and efficacy.

TA criterion 2 is not met.

Level of Evidence: 5

TA Criterion 3

Pathological Study

In a histopathological study, Corica and colleagues (2000) evaluated the thermal ablation pattern in human prostatic tissue after treatment with WIT. Twenty-seven men scheduled for surgery for symptomatic BPH or adenocarcinoma of the prostate underwent WIT. Prostates were subsequently enucleated or removed at a mean of 27 days (range 4 to 120 days) and examined pathologically. Treated patients reported mild treatment discomfort, which did not correlate with balloon diameter, water temperature, or the extent of necrosis. Distal penile burning was the most commonly reported side effect. All patients voided successfully within 12 days of treatment. Pathologic findings included periurethral hemorrhagic necrosis, with focal or extensive uroepithelial denudation and mild inflammation. The mean maximal depth of necrosis from the urethral lumen was 7-11 mm. The extent of necrosis was unrelated to water temperature but did correlate with the balloon diameter. The authors concluded that tissue ablation by WIT was well tolerated, and produced consistent pathologic results.

Clinical Trial

In a prospective multicenter clinical trial, Muschter et al (2000) evaluated the effectiveness and safety of water-induced thermotherapy. A total of 125 carefully selected patients with symptoms due to BPH were enrolled at 8 study sites. Measurements included International Prostate Symptom Score (I-PSS), peak urinary flow rate and quality of life score, and sexual function questionnaire prior to, and at 3, 6 and 12 months after, the WIT procedure.
Clinical Trial, continued

In 4 patients, the catheter could not be inserted due to hypertrophy of the median lobe, 3 patients underwent subsequent TURP, and 6 others were lost to follow-up. Overall, 5.6% of patients were classified as treatment failures. In the remaining 112 patients, comparisons of pre- and post-measures demonstrated significant improvements in I-PSS, peak urinary flow rate and quality of life score. At 12 months, I-PSS had improved by a median of 12.5 (95% CI 11.5, 13.5) versus baseline, peak urinary flow rate by 6.4 ml. per second (95% CI 5.6, 7.5) and quality of life score by 2.5 (95% CI 2.0, 2.5). These favorable effects on I-PSS, peak flow rates, and post-void residuals persisted to 24 months (in 98 patients), and to 36 months, although a total of 8 (8.2%) patients underwent TURP for persistent symptoms by then (Muschter et al, 2000; Schrorsch et al, 2000; Muschter et al, 2001).

At 12 months, no adverse impact on sexual function was noted. Most patients required an indwelling urinary catheter for less than two weeks after the procedure for transient urinary obstruction attributed to thermally induced edema and tissue sloughing. Other adverse events included urinary tract infection or bacteriuria (32.8%), prolonged (> 1 month) or hematuria (22.4%) or dysuria (11.2%), epididymitis (3.2%), transient urinary urge incontinence (2.4%), transient impotence (1.6%), and urinary retention subsequent to post-treatment catheterization (12%) (Muschter et al, 2000).

The authors concluded that WIT could significantly alleviate lower urinary tract symptoms of BPH, increase peak urinary flow rate and enhance patient quality of life, with relatively infrequent and manageable side effects (Muschter et al, 2000).

However, without a control group, these results are difficult to interpret. Specifically, as the authors note, the study lacked a sham control arm and thus the results should be viewed as preliminary. Sham (placebo) effects have been noted in studies of other catheter-based thermal treatments for BPH (Blute et al, 1996; de Wildt et al, 1996; Larson et al, 1998). In addition, without comparative trials, it is difficult to know whether WIT is more or less effective than other available therapies for BPH. Finally, with follow-up extending only to 24 months, long-term durability of the effects of WIT is unknown.
TA Criterion 4

The available alternatives to WIT for men with chronic symptoms of BPH are medical therapies including 5-alpha-reductase inhibitors, such as finasteride (Proscar), and alpha-adrenergic receptor blockers, such as terazosin (Hytrin), and surgical therapies such as TURP, TUNA, and transurethral microwave thermotherapy, or other minimally invasive therapies. Because there have been no randomized, sham placebo controlled trials or direct comparisons of water-induced thermotherapy to other established medical or surgical therapies for BPH, it is not yet clear that WIT improves net health outcomes as much as or more than the established alternatives.

Therefore, TA criterion 4 is not met.

TA Criterion 5

In the single published clinical trial, WIT was evaluated in several centers in Germany, Israel, Denmark and the United Kingdom. Whether WIT improves health outcomes for BPH more than existing technologies has not been demonstrated in the investigational setting, let alone under conditions of usual medical practice.

TA Criterion 5 is not met.

RECOMMENDATIONS OF OTHERS

Blue Cross Blue Shield Association

The Blue Cross Blue Shield Association Medical Policy Manual states: “Water-induced thermotherapy may be considered medically necessary as a treatment of benign prostatic hypertrophy.”

California Urological Association

The California Urologic Association (CUA) has provided the following statement: “The CUA supports the use of Water Induced Thermotherapy as an appropriate viable alternative treatment for symptomatic Benign Prostatic Hypertrophy in accordance with the published California Medicare LMRP on WIT”. The CUA will be represented at the meeting.
CMS (Center for Medicare and Medical Services)

National Heritage Insurance Company (NHIC), the local carrier providing coverage for Medicare services in California adopted the following LMRP on January 15, 2002:

“Water Induced Thermotherapy (WIT) is indicated for the treatment of significant benign prostate hyperplasia or Benign Prostatic Hypertrophy (BPH) causing an American Urological Association (AUA) symptom index score of 11 or higher indicating moderate symptoms with compromised quality of life which has been present for more than 3 months and failure of a reasonable trial of medical therapy OR, an AUA symptom score over 19.”

CONCLUSION

Water-induced thermotherapy holds promise as a useful option for the clinical management of BPH. A single prospective, uncontrolled study of WIT showed improvement in both urinary flow and symptom scores at 12 to 24 months follow-up. Because WIT is a low-morbidity and anesthesia-free outpatient procedure, it is an attractive alternative in the treatment of patients in chronic BPH, especially those patients who are poor surgical risks. However, randomized sham placebo-controlled or comparative studies, and long-term follow-up studies, of its efficacy and complications are still lacking. Existing studies have not yet demonstrated that WIT results in better health outcomes as much as or more than the established alternative of TURP, TUNA, or microwave thermotherapy. It is also unclear if its benefits could be achieved under conditions of usual medical practice or with less carefully selected patients. Therefore, TA criteria 2-5 are not met.

RECOMMENDATION

It is recommended that transurethral water-induced thermotherapy of the prostate for benign prostatic hyperplasia does not meet Blue Shield TA criteria.

Committee approval as recommended

February 13, 2002
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