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Development of Feedback Microwave Thermotherapy in Symptomatic Benign Prostatic Hyperplasia.

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2006

[Link to publication](#)

Citation for published version (APA):

Schelin, S. (2006). *Development of Feedback Microwave Thermotherapy in Symptomatic Benign Prostatic Hyperplasia*. [Doctoral Thesis (compilation), Urology]. Department of Urology, Clinical Sciences, Lund University.

Total number of authors:

1

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Mediating Transurethral Microwave Thermotherapy by Intraprostatic and Periprostatic Injections of Mepivacaine Epinephrine: Effects on Treatment Time, Energy Consumption, and Patient Comfort

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ABSTRACT

Background and Purpose: Profound intraprostatic blood flow may complicate reaching a therapeutic temperature in the prostate during transurethral microwave thermotherapy (TUMT) for benign prostatic hyperplasia (BPH). A retrospective survey is presented describing the effect of intraprostatic and periprostatic administration of mepivacaine epinephrine on treatment time, intraprostatic blood flow, energy delivery, and patient comfort.

Patients and Methods: Fifteen consecutive obstructed patients with lower urinary tract symptoms attributable to BPH received TUMT (ProstaLund Feedback Treatment®). In order to improve patient comfort, injections of 10 mL of 0.5% mepivacaine epinephrine were administered in three locations into the prostate prior to treatment. The results were compared with those of a reference group consisting of 35 consecutive patients who had received ProstaLund Feedback Treatment without administration of mepivacaine epinephrine.

Results: Patients who received intraprostatic mepivacaine epinephrine had a shorter treatment time (32 ± 9 minutes ν 61 ± 6 minutes), required less energy (65 ± 27 kJ ν 172 ± 32 kJ), and had a lower calculated intraprostatic blood flow (13 ± 5 units/minute ν 26 ± 12 units/minute) than the reference group. Patients receiving mepivacaine epinephrine also required less analgesic medication during the treatment. The clinical outcome in terms of symptom scores and peak uroflow rates appeared to be similar for the two groups.

Conclusion: Intraprostatic injection of mepivacaine epinephrine prior to TUMT seems to have beneficial effects. It may represent an important improvement of thermotherapy and enable successful treatment of those patients who previously failed secondary to a profound intraprostatic blood flow.

INTRODUCTION

TRANSURETHRAL MICROWAVE THERMOTHERAPY (TUMT) is considered one of the most promising minimally invasive therapies for benign prostatic hyperplasia (BPH).¹ Recently, the International Consultation on Urological Diseases (ICUD) stated at the 5th International Consultation on Benign Prostatic Hyperplasia 2000 that "microwaves have undoubtedly turned the period of adolescence, without the descending slope that other, initially promising modalities, have shown."² Several clinical studies have demonstrated TUMT to

be a safe and efficient treatment both in patients with mild to moderate obstruction³ and in patients in persistent urinary retention.⁴⁻⁶ The success rate has been reported to be in the range of 60% with conventional TUMT and as high as 82% with the newly developed ProstaLund Feedback Treatment® (PLFT®), a method that is guided by the actual intraprostatic temperature.^{7,8}

Clearly, the intraprostatic temperature achieved is important in obtaining tissue necrosis and a satisfactory clinical outcome.^{7,9} The intraprostatic temperature is determined mainly by the applied microwave energy and the intraprostatic blood

flow, although variations in tissue composition may also interfere.¹⁰ It may be speculated that patients who respond poorly to TUMT have a profound intraprostatic blood flow acting as a heat sink, so that therapeutic intraprostatic temperatures are not reached. Local injections into the prostate of a vasoconstrictor drug prior to treatment thus might be useful to lower the intraprostatic blood flow and thereby facilitate the intraprostatic temperature rise during TUMT.

To further investigate this hypothesis, a retrospective survey was performed on 15 consecutive patients who had received intraprostatic administration of local anesthetics with epinephrine (mepivacaine epinephrine) prior to TUMT with the PLFT in order to improve patient comfort during treatment. The results were compared with those of 35 consecutive patients who had received the same TUMT except for the intraprostatic administration of local anesthetics.

PATIENTS AND METHODS

Fifteen consecutive and unselected TUMT sessions were analyzed retrospectively by reviewing medical records. The reason for TUMT was outflow obstruction by BPH. All 15 patients had received intraprostatic administration of mepivacaine epinephrine prior to the TUMT in order to improve patient comfort during treatment. For comparison, the same analysis was performed on 35 consecutive TUMT sessions performed on patients who had not received any intraprostatic injection of mepivacaine epinephrine prior to treatment (reference group). All patients in both groups had the same work-up prior to treatment; i.e., prostate specific antigen assay, kidney function tests, urine culture, International Prostate Symptom Score (IPSS), free urine flow (Q_{max}), bother score, residual urine measurement, and transrectal ultrasound (TRUS) examination for prostate volume determination. None of the patients was tried on alpha-blockers before TUMT. All patients were treated in the office. High-risk patients (ASA 3 and 4) were always excluded, being referred for treatment under anesthesiology supervision at the hospital.

Microwave Thermotherapy

The thermotherapy was administered using the ProstaLund Compact device with PLFT that is guided by the actual intraprostatic temperature. The intraprostatic temperature is continuously measured by means of a probe with multiple thermosensors that protrude from the transurethral treatment catheter into the prostate during the treatment. By using Penne's bioheat model,¹¹ the system continuously estimates the intraprostatic blood flow index and the size of the zone of coagulation necrosis.^{12,13} The estimated size of the zone of necrosis is used to determine the endpoint of the treatment.¹² The treatment objective is usually to coagulate 20% to 30% of the baseline prostate volume, depending on the degree of prostatic enlargement. Normally, an intraprostatic temperature in the range of 50°C to 60°C is required to achieve the desired necrosis.

General Medication

All patients received 5 mg of diazepam intravenously and 25 mg of emeprom bromide intramuscularly as standard med-

ication prior to treatment. Additional diazepam, pethidine (meperidine), or both were administered on demand during the treatment.

Intraprostatic Injection

The injections of mepivacaine epinephrine were given by the transurethral route with a catheter device. The catheter had a balloon at the tip that made it possible to anchor it at the bladder neck. A cannula 1.2 mm in diameter was guided through a separate channel inside the catheter and protruded from the catheter at the level of the prostate. At a 30° angle, the cannula penetrated the prostate to a depth of 45 mm, reaching the base of the gland in the 4 and 8 o'clock positions, and regularly penetrated the prostatic capsule in the 12 o'clock position. This device enabled easy medication of the prostate blindly by the transurethral route under aseptic conditions. Three injections (10 mL each) of 0.5% mepivacaine epinephrine were administered at 4, 8, and 12 o'clock, according to the entrance of the major blood vessels (Fig. 1). Each injection was performed by injecting 5 mL when the cannula was fully introduced in the deep position. Thereafter, 5 mL was administered as infiltration anesthesia while the cannula was retracted. Each injection was preceded by aspiration to avoid intravascular injection. Analgesia with intraprostatic injection of mepivacaine epinephrine was established as a clinical routine to improve patient comfort during TUMT.

The reference group consisted of patients who received TUMT before this routine was established. Thus, no selection was made whether a patient should receive mepivacaine epinephrine or not.

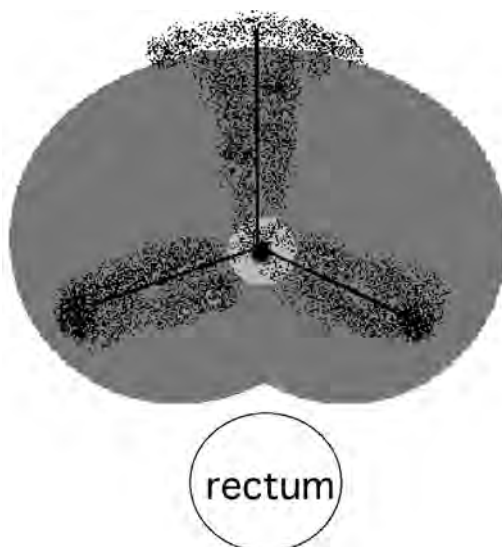


FIG. 1. Transverse section of prostate showing location of injections of mepivacaine epinephrine. Shaded area indicates expected drug distribution.

TABLE 1. TREATMENT VARIABLES FOR REFERENCE GROUP AND GROUP RECEIVING INTRAPROSTATIC MEPIVACAINE EPINEPHRINE

	Reference (N = 35) Mean (SD)	ME (N = 15) Mean (SD)
Treatment time (min)	61 (6)	32 (9)
Energy (kJ)	172 (32)	65 (27)
Intraprostatic blood flow (units/min)	26 (12)	13 (5)
Estimated tissue necrosis (g)	18.9 (10.3)	14.3 (7.3)
Intraprostatic max temperature (°C)	56.1 (4.5)	57.1 (2.6)

Data

The data are presented as mean \pm SD.

RESULTS

In patients who had received intraprostatic injection of mepivacaine epinephrine prior TUMT, the treatment duration was 32 ± 9 minutes compared with 61 ± 6 minutes for patients who had not received mepivacaine epinephrine prior to treatment (Table 1). In accordance, the amount of microwave energy required for the treatment was reduced by 62% in the mepivacaine epinephrine group compared with the reference group. Furthermore, the intraprostatic blood flow, as estimated by PLFT, was reduced by 50% in the mepivacaine epinephrine group compared with the reference group. The maximal intraprostatic temperature during the treatment was 57.1°C in the mepivacaine group and 56.1°C in the reference group. For the mepivacaine group, the achieved tissue necrosis was estimated to 14.3 g. The corresponding figure for the reference group was 18.9 g.

The two groups had similar improvements in clinical outcome at the regular follow-up visit approximately 3 months post-treatment. The IPSS and bother score in the mepivacaine group improved by 72% and 82%, respectively (Table 2). The corresponding figures in the reference group were 71% and

82%, respectively. In accordance, the peak uroflow rate increased by 68% in the mepivacaine group and 78% in the reference group. A considerable prostate volume reduction was seen on TRUS 3 months post-treatment in both groups, the reduction being 35% in the mepivacaine group and 29% in the reference group. No side effects attributable to the mepivacaine epinephrine administrations were noted except asymptomatic tachycardia (90–120/min), which subsided within 15 minute. No sequelae occurred.

Analysis of concomitant administration of analgesic and sedative medication (except intraprostatic injections of mepivacaine epinephrine) prior to or during the treatment demonstrated that the mepivacaine group had received an average of 5.3 mg of diazepam/patient (median 5 mg/patient) prior to or during the treatment. The reference group had received on average 9.2 mg of diazepam/patient (median 10 mg/patient). A similar pattern was found for pethidine administration. Pethidine was given to the mepivacaine group with an average of 2.7 mg/patient (median 0 mg/patient), while the reference group received an average of 13.8 mg/patient (median 15 mg/patient).

DISCUSSION

This retrospective survey reveals that intraprostatic and periprostatic administration of mepivacaine epinephrine prior

TABLE 2. IPSS, BOTHER SCORE, PEAK UROFLOW, AND PROSTATE VOLUME AT BASELINE AND 3 MONTHS AFTER PLFT FOR REFERENCE GROUP (REF) AND GROUP RECEIVING INTRAPROSTATIC MEPIVACAINE EPINEPHRINE (ME)

	Baseline		3 months	
	Mean (SD)	No.	Mean (SD)	No.
IPSS				
Ref	22.8 (6.3)	31	6.7 (5.5)	31
MA	19.8 (6.2)	13	5.6 (3.0)	12
Bother score				
Ref	3.9 (1.0)	31	0.7 (0.9)	31
MA	3.9 (1.4)	11	0.7 (1.0)	12
Peak flow (mL/sec)				
Ref	7.3 (2.6)	25	13.0 (4.6)	25
MA	8.5 (2.2)	10	14.3 (4.6)	9
Prostate weight (g)				
Ref	61.7 (26.2)	35	43.7 (19.2)	35
MA	60.4 (26.5)	15	39.4 (10.1)	10

to TUMT results in a shorter treatment time with treatments utilizing less microwave energy. Most probably, this is an effect of reduced intraprostatic blood flow attributable to the vasoconstrictor effect of mepivacaine epinephrine. Those results are also supported by the fact that the intraprostatic blood flow in the mepivacaine group, as estimated by PLFT,¹² was <50% of that in the reference group. The reduced intraprostatic blood flow decreases heat transport out of the prostate and thereby facilitates the temperature rise in the gland. Accordingly, the maximal intraprostatic temperature was in the same range for both treatment groups, although the mepivacaine group utilized 62% less microwave energy than the reference group.

The importance of the blood flow and vascularity has previously been discussed, and computer modeling experiments have shown that variation in the intraprostatic blood flow has a considerable impact on the intraprostatic temperature.¹⁴ In addition, Floratos and Aarnink¹⁰ concluded that the role of intraprostatic vascularity as a regulator of temperature during the treatment seems to be of greatest importance. Experience from TUMT with PLFT shows that there are considerable interindividual variations in intraprostatic blood flow. There is also a pronounced variation in one individual during treatment: the blood flow often increases twofold or more in response to heat exposure, probably a consequence of a defense mechanism. After some 20 to 45 minutes, the prostatic blood flow suddenly decreases significantly, probably secondary to the build-up of intraprostatic edema in the heated area and perhaps also to microthrombosis. In this phase of the treatment, the intraprostatic temperature begins to rise, and coagulation necrosis is developing rapidly. Patients who received mepivacaine epinephrine prior to PLFT did not appear to have this initial increase in blood flow, and the formation of tissue necrosis appeared to start earlier.

To the best of our knowledge, this is the first report describing a method to decrease the intraprostatic blood flow pharmacologically in order to facilitate TUMT. However, intraprostatic injection of local anesthetics has previously been described in attempts to perform transurethral resection (TURP) as an office procedure. In these studies, the drug has been administered by the transurethral¹⁵ or perineal^{16,17} route or a combination.¹⁸ A considerable analgesic effect has been achieved that enabled TURP to be carried out without general or regional anesthesia. Consequently, intraprostatic injection of local anesthetics seems to have a potent analgesic effect during prostate surgery.

A review of the analgesic and sedative drugs given prior to and during the treatment in the current survey also indicates that mepivacaine epinephrine has an analgesic effect and that it improved patient comfort during TUMT. The majority of the patients in the mepivacaine group did not receive more than the one initial dose of diazepam. In contrast, most patients in the reference group received additional diazepam during the treatment, frequently in combination with pethidine.

The data reported in this survey indicate that intraprostatic and periprostatic injection of mepivacaine epinephrine prior to TUMT with PLFT may represent an important improvement of thermotherapy and ought to be the target of further investigations. The method may enable successful treatment of those patients who previously failed because of profound intraprostatic blood flow. A randomized study needs to be performed in order to evaluate the method further. The method may also rep-

resent an interesting application for TURP, in addition to the analgesic effect as reported previously.¹⁵⁻¹⁸ A considerable reduction of the intraprostatic blood flow during TURP may decrease the bleeding and thereby improve the safety and facilitate the procedure.

CONCLUSION

Intraprostatic and periprostatic injection of mepivacaine epinephrine prior to TUMT seems to have beneficial effects on treatment time, required energy, intraprostatic blood flow, and patient comfort. This method may represent an important improvement in microwave thermotherapy.

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