TRANSURETHRAL DEHYDRATED ETHANOL INJECTION OF THE PROSTATE FOR THE TREATMENT OF BENIGN PROSTATIC HYPERPLASIA (BPH): A PRELIMINARY REPORT

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Abstract

Purpose To evaluate the efficacy and safety of a minimally invasive treatment for benign prostatic hyperplasia (BPH) by transurethral dehydrated ethanol injection.

Patients and method Eight patients with clinical symptoms of benign prostatic hyperplasia were evaluated by urodynamic study, cystoscope and transrectal ultrasound preoperatively. Under regional anesthesia, transurethral injection was performed at 6-10 sites into median and bilateral prostatic lobes, and 12-20 mL of dehydrated ethanol was used depending on the prostatic size in each patient. At 3 months after treatment, International prostatic symptom score (IPSS), quality of life score and parameter of benign prostatic obstruction (BPO) were re-evaluated and compared with the baseline.

Result Average operative time was 19.29 minutes (range 15-30). There were no intraoperative complications, but the postoperative treatment required catheterization for a mean of 11 days (range 7 to 39). Gross hematuria and blood clot obstruction had caused irrigate bladder to occur in 1 patient. Only 1 patient could not remove the urethral catheter in 4 weeks, so he was offered transurethral resection of the prostate. Seven patients completed the study. The median IPSS was 23 (range 16 to 31) preoperatively, and it significantly improved to 5 (range 2 to 17) at 3 months postoperatively ($p=0.018$). The median quality of life score also improved significantly from 5 (range 4 to 6) to 1 (range 0 to 2) ($p=0.016$). The mean residual urine volume significantly decreased from 103.71±70.88 to 21.29±18.36 mL ($p=0.016$). However, the mean peak urinary flow rate increased, but not significantly, and there was no significant change in mean prostate volume from 39.30±28.11 to 28.44±12.90 mL ($p=0.241$).

Conclusion Our preliminary data proved that this technique is an effective alternative treatment with minimal adverse effects, and it is safe for patients with benign prostatic hyperplasia, especially when there is a high operative risk. Chiang Mai Med J 2007;46(2):67-74.

Keywords: prostatic hyperplasia, ethanol injection, quality of life, urodynamics
Benign prostatic hyperplasia (BPH) is one of the most common diseases in aging males. It causes chronic and progressive lower urinary tract symptoms that affect quality of life by interfering with daily activities and sleep patterns. The goal of therapy is to improve lower urinary tract symptoms and quality of life, prevent severe BPH related complications and minimize the adverse effects of the treatment. The treatment options include watchful waiting, and medical and surgical treatment depending on the severity of symptoms. Transurethral resection of the prostate (TUR-P) has been the gold standard of surgical treatment for BPH for many decades, however, this procedure may cause serious complications, especially in old aged men with high cardiovascular risk. In recent years, many kinds of less invasive techniques have been developed for minimizing complications, while the patients can achieve satisfactory results from in relieving symptoms.

Ethanol injection therapy has previously been used for liver and thyroid tumors.\(^{1,2}\) In 1999, Goya N, et al\(^{3}\) demonstrated the efficacy of transurethral ethanol injection therapy of the prostate for BPH. The 2004 consensus of the European Association of Urology (EAU) on the management of BPH reported that transurethral injection of absolute ethanol into the prostate, resulting in coagulation necrosis (chemo-ablation), was the emerging therapy.\(^{4}\) The aim of this study was to evaluate the feasibility, safety and efficacy of transurethral dehydrated ethanol injection therapy in BPH.

**Material and methods**

This study was conducted at the Division of Urology, Department of Surgery, Chiang-Mai University. The institutional ethics committee approved the protocol for this before-after treatment study.

Men over 50 years of age, who had symptomatic BPH, were enrolled from May 2004 to March 2005 after informed consent was obtained. The International prostatic symptom score (IPSS) was used to assess the degree of urinary symptoms. The total score reflected the overall severity of BPH (score 1 to 7, mild symptoms; 8 to 19, moderate; and 20 to 35, severe). The quality of life (QoL) was scored by using IPSS (from score 0, the most satisfaction to score 5 the worst disturbance). All patients underwent a digital rectal examination, urine analysis and serum concentration of prostate-specific antigen (PSA) test to exclude other lower urinary tract and prostatic diseases. In addition, the criteria for benign prostatic obstruction were confirmed by the Urodynamic study, and transrectal ultrasonography (TRUS) was used to determine the prostate volume.

After a baseline evaluation, ethanol injection therapy of the prostate under regional anesthesia was performed. Using a 6 French 50 cm long needle via rigid cystoscope into the prostate under direct vision, 2.0 mL of dehydrated ethanol per site were injected transurethrally at 4 to 8 sites in the right, left and median prostatic lobe, depending on the size and character of the prostate. However, the total amount of ethanol used was not more than 25 mL in each patient. A Foley’s catheter was inserted after completion of the procedure. The catheter was removed after seven days.

The operative outcome assessment by subjective evaluations including IPSS, quality of life score and adverse event was done at 6 and 12 weeks postoperatively. In addition, objective evaluations with the Urodynamics study and transrectal ultrasound of prostatic
size were assessed at 12 weeks postoperatively.

**Statistical analysis**

All statistical analyses were obtained by using SPSS 10.0. The results were expressed as a median and range or mean ± standard deviation. The clinical data of pre and post-treatment IPSS and quality of life score were compared by using the Wilcoxon signed rank test. Urodynamic parameter and prostatic size were compared by the Paired t-test. A $p < 0.05$ was considered statistically significant.

**Result**

A total of 8 patients were recruited. The mean patient age was 70.29±10.03 years (range 55 to 84). A severe aortic regurgitation presented in 1 patient, 1 had chronic obstructive pulmonary disease, and another one had cirrhosis. After treatment with transurethral dehydrated ethanol injection, only 1 patient had refractory urinary retention after removal of the catheter 4 weeks postoperatively. He requested termination of the study protocol, and so transurethral resection of the prostate (TUR-P) was done afterwards. This patient was excluded from the study evaluation.

Seven patients, who completed the study protocol, presented with a median preoperative symptom score of 23 (range 16 to 31) and their median quality of life score was 5 (range 4 to 6). The preoperative mean peak urine flow rate was 5.29±3.82 mL per second (range 0 to 10) and the mean residual urine volume was 103.71±70.88 mL (range 10-200). Mean detrusor pressure at maximum flow was 79.00±24.61 cmH2O, and the mean Abrams-Griffiths number was 68.43±28.41 preoperatively. The mean estimate of prostate volume was 39 mL (range 13.15 to 85.80). The mean number of injection sites was 7.86 per person (range 6-10) and the mean total volume of ethanol injected was 15.71 mL (range 12 to 20).

The average operative time was 19.29 minutes (range 15-30) and the average length of hospital stay was 2.71 days (median of 2 days, range 2-6). There were no changes in blood pressure, pulse rate or symptoms of alcohol toxicity in any patients during the procedure. Minor bleeding occurred in all patients, but in most of them it was spontaneously resolved without a significant decrease in hematocrit. Only 1 patient had blood clot retention and required irrigate bladder. The mean time for urethral catheter removal was 11 days (7 to 39).

The results of the preoperative and postoperative subjective assessments are shown in Figure 1 and 2. At 6 weeks, the median symptom score had decreased to 10 (range 5 to 19) and median quality of life decreased to 1 (range 1 to 2). All 7 patients were satisfied with their urinary tract symptoms. At 3 months, the median symptom score had decreased to 5 (range 2 to 17), $p=0.018$, and median quality of life score was 1 (range 0 to 2), $p=0.016$. The change in symptom score and quality of life score were significantly improved at 3 months compared to the baseline value ($p<0.05$).

The results of the preoperative and postoperative objective assessments are shown in Table 1. The residual urine volume had decreased significantly at 3 months after treatment ($p<0.05$). The peak urine flow rate increased, but not significantly ($p=0.13$). Other Urodynamic parameters, which were references of bladder outlet obstruction such as detrusor pressure at maximum flow and Abrams-Griffiths number, decreased to a value near to the normal limit, but with no statistical
Figure 1. IPSS improvement.

Figure 2. Quality of life score improvement.

Table 1. Changes in urodynamic characteristics and prostate measurements at baseline and 12 weeks after prostate dehydrate ethanol injection

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Baseline</th>
<th>12 weeks</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detrusor pressure at Q-max (cm H2O)</td>
<td>79.00±24.61</td>
<td>62.29±25.32</td>
<td>0.159</td>
</tr>
<tr>
<td>Maximal urine flow rate (mL/s)</td>
<td>5.29±3.82</td>
<td>8.43±3.78</td>
<td>0.130</td>
</tr>
<tr>
<td>Abrams-Griffiths number</td>
<td>68.43±24.41</td>
<td>41.51±29.40</td>
<td>0.059</td>
</tr>
<tr>
<td>Post void residual urine volume (mL)</td>
<td>103.71±70.88</td>
<td>21.29±18.36</td>
<td>0.016</td>
</tr>
<tr>
<td>Total prostate volume (mL)</td>
<td>39.30±28.16</td>
<td>28.44±12.90</td>
<td>0.241</td>
</tr>
</tbody>
</table>

Data presented as the mean ± SD
Ethanol injection for prostatic hyperplasia

significance. \( p=0.159 \) and \( p=0.059 \) respectively) The average prostate size also decreased from 39.3 to 28.44 mL, but with no statistical significance.

Of post operative complications, acute urinary retention occurred in 1 patient, and gross hematuria in another one. Both of these patients were managed by temporary indwelling catheterization for 3-5 days, which enabled them to urinate with no problem. One patient had acute epididymo-orchitis and responded well with oral antibiotics.

Discussion

The aim of BPH treatment is to improve urinary tract symptoms, quality of life and prevention of severe BPH-related complications. Traditionally, medical therapy, such as alpha-adrenergic blocking agent and 5 alpha-reductase inhibitor, was the first line treatment for patients with moderate to severe lower urinary tract symptoms that significantly disturbed their quality of life. Some patients, who did not respond to medical therapy or have BPH related complication, needed surgical treatment. Transurethral resection of the prostate (TUR-P), transurethral incision of the prostate (TUI-P) and open prostatectomy are the conventional surgical options. However, the surgical side effects of these operations were a major consideration that prompted the search for a minimally invasive technique, which could relieve symptoms, while proving cost effective and avoiding troublesome complications.

Absolute ethanol has been used for tissue ablation and nerve blockade with great success over the last few decades. It produced coagulated necrosis in many kinds of tumors such as hepatocellular carcinoma\(^{(1)}\) and thyroid adenoma.\(^{(2)}\) The feasibility of injection therapy for benign prostate hyperplasia has also been explored. The studies in animals demonstrated the safety and efficacy of absolute ethanol injection of the prostate.\(^{(5-7)}\) Histological sections of the prostate at 6 months after injection showed fibrosis and scarring, with glandular atrophy resulting in a widened urethral lumen.\(^{(5,6)}\) In humans, Goya N, \textit{et al}.\(^{(3)}\) who first described the ethanol injection for benign prostatic hyperplasia in 10 patients, reported a decrease in symptom score from 23.1 to 12.2, an improvement in quality of life score from 5.1 to 3.2 at 3 months postoperatively, an increase in peak urine flow rate from 8.0 to 13.1 mL per second and a decrease in residual urine volume from 129.1 to 49.3 mL at 3 months postoperatively. There was no significant change in prostate volume. A recent study by Ditrolio \textit{et al}\(^{(8)}\) used an InjectTx endoscopic device for transurethral injection of absolute ethanol, which also demonstrated successful results. However, postoperative catheterization was required for an average of 3.6 days (range 3 to 10). Gross hematuria was present in all patients for 2 to 3 days. Chiang PH, \textit{et al}\(^{(9)}\) reported an alternative technique to ethanol injection. They used a transrectal ultrasound guide for transperineal injection in 11 patients with prostatic obstruction, due to benign prostatic hyperplasia or prostate cancer. The mean symptom score decreased from 17.7 to 8.5, the mean peak urine flow rate increased from 5.3 mL/s to 13.5 mL/s, and the mean residual urine volume decreased from 231.9 mL to 28.7 mL at 3 months postoperatively.

Our preliminary results showed a significant improvement in symptom score, quality of life score and post voiding residual urine, while other parameters had changed but not significantly improved. However, the obstructive parameters such as peak urine flow rate, detrusor pressure at max flow, and Abrams-
Griffiths number did not reach the levels achieved after transurethral resection of the prostate (TUR-P), which was the gold standard for treating benign prostrate hyperplasia. These results were explained by the reduction in prostatic volume after the ethanol injection in our series showed no significant difference, while the transurethral resection of prostate (TUR-P) could remove the prostate tissue, which was causing obstruction at a significant rate. Alpha adrenergic receptors were the possible mechanism underlying the effect of ethanol injection therapy, which improved the urinary symptoms, while the size of the prostate did not decrease. The alpha1-adrenergic mediated contraction of smooth muscle cells within the prostate, prostate capsule and bladder neck resulted in increasing bladder outlet resistance in patients with BPH. After use of the alpha adrenergic blocking agents for treating BPH, the symptom scores improved by 4-6 points, and the maximal urine flow rate by 2-3 mL/s.\(^{(4)}\) The alpha1-blockers had no effect on prostate volume and did not prevent further prostate growth. The alpha1-receptors may be destroyed by ethanol, thus decreasing the tone of the prostatic urethra, resulting in relief from obstruction. In our study, improved obstruction was demonstrated, but not significantly. The long-term outcome of this therapy also needs to be determined by following a larger series of patients.

Transurethral ethanol injection of the prostate was a relatively simple procedure that could be completed in about half an hour, and it had no serious intraoperative complications such as trans urethral resection (TUR) syndrome. Some investigators\(^{(1,8,9)}\) suggested that this procedure could be done in an outpatient facility without hospitalization or with only an overnight stay in hospital. Hematuria alone usually occurred in the post operative period, but it was resolved spontaneously in a few days. Some patients needed urethral catheterization to prevent urinary retention after the procedure, due to an inflammatory process from tissue reaction to ethanol. However, almost all patients could urinate satisfactorially in 7 days postoperatively. Goya et al, assessed medium term efficacy of this treatment and reported that 59% of their patients had not required medication or further treatment, and they were satisfied with the outcome by 3 years after surgery.\(^{(10)}\) With respect to cost-effectiveness, in comparison to long-term medication for BPH, the use of lifelong, transurethral ethanol injection of the prostate has the potential to be a minimally invasive, safe and inexpensive option that provides satisfactory results.

**Conclusion**

The results of this study have demonstrated that prostate injection of dehydrated ethanol for bladder outlet obstruction, due to benign prostatic hyperplasia, is an effective alternative treatment with minimal side effects for patients with BPH obstruction, especially in those with high operative risk. The procedure is safe and well tolerated.

**Acknowledgement**

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**References**


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Ethanol injection for prostatic hyperplasia


การรักษาต่อมลูกหมากโตโดยวิธีฉีดเอธิลแอลกอฮอล์บริสุทธิ์ผ่านทางท่อปัสสาวะ

ศุภณ ศรีพลากิจ, พิเศษ อินสวน, พิเศษ บิริ

บทคัดย่อ

วัตถุประสงค์ เพื่อประเมินประสิทธิภาพและความปลอดภัยของการใช้เอธิลแอลกอฮอล์บริสุทธิ์ฉีดดัดต่อมลูกหมากผ่านทางท่อปัสสาวะเพื่อรักษาต่อมลูกหมากโต

ผู้ป่วยและวิธีการรักษา ผู้ป่วยจำนวน 8 ราย ที่มีอาการของต่อมลูกหมากโตได้รับการประเมินอาการโดยใช้ IPSS (international prostatic symptom score) ตรวจสอบการผ่าตัดความเสี่ยงการผ่าตัดและการตรวจวัดระดับยาที่ใช้ในผู้ป่วย ผู้ป่วยทุกรายจะได้รับการฉีดเอธิลแอลกอฮอล์บริสุทธิ์เข้าบริเวณต่อมลูกหมากตั้งแต่ 6-10 ตำแหน่ง กระบอกยาทางท่อปัสสาวะ ไม่พบภาวะแทรกซ้อน เพื่อมีการเลือกต่อมลูกหมากในมุมที่最适合 ผู้ป่วยจะได้รับการประเมินหลัง 3 เดือน โดยใช้ IPSS และการตรวจยูโรพลศาสตร์เพื่อประเมินผลและหลังได้รับการรักษา

ผลการศึกษา ระยะเวลาการผ่าตัดโดยเฉลี่ยประมาณ 19.29 นาที (ตั้งแต่ 15-30 นาที) ไม่พบภาวะแทรกซ้อนที่เห็นได้ชัดเจน แสดงถึงผู้ป่วยจะมีสุขภาพที่ดีเป็นต้องการสำหรับการทำให้ปัสสาวะกลับค้างได้ เฉลี่ย 11 วัน (ตั้งแต่ 7-19 วัน) พบผู้ป่วย 1 ราย ไม่สามารถปัสสาวะออกได้ภายในระยะเวลา 4 วัน เนื่องจากไม่สามารถปัสสาวะได้หลังการผ่าตัด ผู้ป่วยรายนี้มีอาการหอบหืมและหายใจลำบาก ผู้ป่วยรายนี้มีการตรวจยูโรพลศาสตร์ ไม่พบภาวะแทรกซ้อน แต่หลังผ่าตัดผู้ป่วยจำเป็นต้องใส่สายสวนปัสสาวะ ตั้งแต่ 7-39 วัน โดยที่เฉลี่ย 11 วัน พบผู้ป่วย 1 ราย  얘ก็มีการผ่าตัด IPSS ส่วนการตรวจยูโรพลศาสตร์ ผู้ป่วย 23 หลังจากได้รับการรักษา พบว่าผู้ป่วยมีการดีขึ้นอย่างมีนัยสำคัญ ดังนี้ IPSS จาก 23 ลดลงเหลือ 5 (p=0.018) และค่าดัชนีชี้วัดคุณภาพชีวิตของผู้ป่วยหลังใต้การรักษาดีขึ้นจาก 5 เหลือ 1 (การรักษาดังกล่าวทำให้มีการเปลี่ยนแปลงค่าดัชนีชี้วัดที่มีนัยสำคัญต่างกัน) ค่าเฉลี่ยปัสสาวะคงค้างลดลงจาก 103.71 มิลลิลิตร เหลือ 21.29 มิลลิลิตร (p=0.016) อย่างไรก็ตาม ค่าเฉลี่ยเวลาการไหลสูงสุดของปัสสาวะเพิ่มขึ้นอย่างมีนัยสำคัญ แต่ค่าเฉลี่ยมีการเปลี่ยนแปลงอย่างมีนัยสำคัญ

สรุป จากการศึกษาพบว่าการใช้เอธิลแอลกอฮอล์บริสุทธิ์ผ่านทางท่อปัสสาวะเป็นวิธีการรักษาต่อมลูกหมากที่ทั้งมีประสิทธิภาพและมีผลข้างเคียงน้อย ที่มีการเปลี่ยนแปลงมีนัยสำคัญ

คำสำคัญ: ต่อมลูกหมากโต เอธิลแอลกอฮอล์ คุณภาพชีวิต ยูโรพลศาสตร์