The Efficacy of Thai Capsaicin in Management of Overactive Bladder and Hypersensitive Bladder

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Abstract

This paper has been generated to provide information on the effectiveness of capsaicin treatment among patients with overactive or hypersensitive bladder. The evaluation process required approximately 14 (overactive bladder) and 11 (hypersensitive bladder and primary detrusor instability) participants who received capsaicin intravesically. The solution consisted of capsaicin (concentration = 1 mM/L) diluted in 30 per cent ethanol solution 100 ml. All participants went through at least 1 urodynamic test 1 month before and after receiving capsaicin intravesical instillation.

The capsaicin treatment for overactive and hypersensitive bladders was very effective. On the average, (overactive bladder) participants' voiding needs decreased from 16.5 $\pm$ 4.8 times/day to 8.6 $\pm$ 2.5 times/day, leakage from 9.7 $\pm$ 8.1 times/day to 2.4 $\pm$ 4.3 times/day, bladder capacity from 160.1 $\pm$ 123.3 ml to 236.9 $\pm$ 146.1 ml, and detrusor contraction from 71.1 $\pm$ 29.2 cm/H_2O to 57.3 $\pm$ 27.2 cm/H_2O.

On average, (hypersensitive bladder and primary detrusor instability) participants' voiding needs decreased from (Day time) 19.45 $\pm$ 17.99 times to 12.00 $\pm$ 8.91 times/day, (Night time) 7.09 $\pm$ 6.03 times to 4.09 $\pm$ 3.8 times, bladder capacity from 197.40 $\pm$ 156.06 ml to 323.45 $\pm$ 129.46 ml, and detrusor contraction from 32.64 $\pm$ 22.77 cm/H_2O to 36.64 $\pm$ 19.22 cm/H_2O.

Capsaicin efficiency was rated very high for both overactive and hypersensitive bladder and primary detrusor instability.

In Thailand, it has been possible to produce capsaicin using local chili supplies, thus the price of the drug itself is very economical. When considering the efficiency and the inexpensive cost of capsaicin, this treatment would be another great alternative for overactive and hypersensitive bladder cure.

Key word : Capsaicin, Overactive Bladder, Hypersensitive Bladder

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J Med Assoc Thai 2003; 86: 861-867**

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The term overactive bladder[1] refers to the symptoms of urinary frequency (urinate more than 8 times/24 h), urgency, and/or urge incontinence. In urodynamics, an overactive bladder is the cause of involuntary detrusor contractions during the filling phase, which may be provoked by rapid filling, posture alterations and coughing etc. The hypersensitive bladder is the symptom of frequent urination but the urodynamic finding is normal. Patients with an overactive or hypersensitive bladder are unable to control or suppress such symptoms.

Capsaicin is extracted from chili[2]; it is the key element that makes chili hot and spicy. Its scientific name is 8-methyl-N-6-nonenamide. In medical practice, capsaicin has been widely used to reduce pain that is caused by physical tissue damage. It was later tested and introduced to overactive and hyper-sensitive bladder patients.

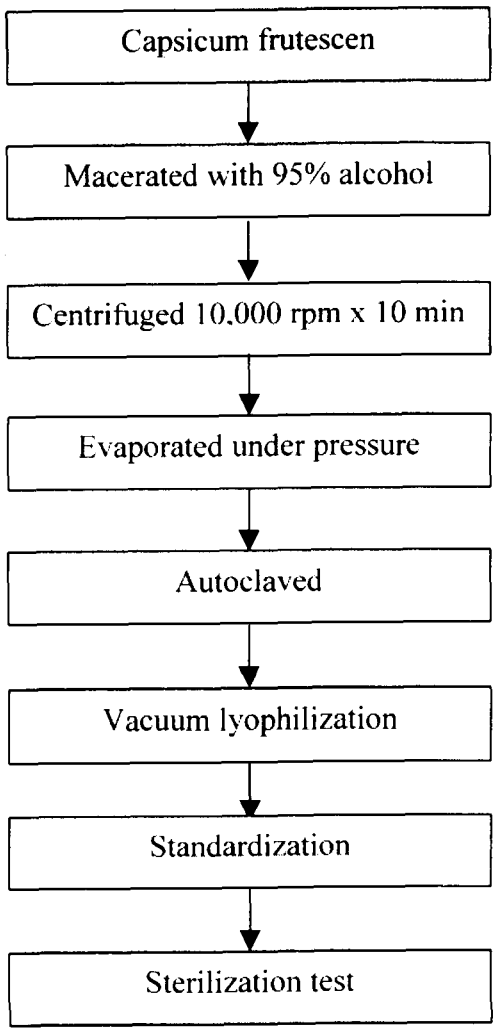
In Thailand, chili is grown nationwide. Based on the abundant natural resource, its inexpensive price, and treatment efficiency, the Siriraj medical team decided to further investigate and develop the usage of capsaicin for future benefits and purposes.

Study procedures

In the present experiment, the Siriraj team used a self-controlled prospective study. The sample group of overactive bladder participants consisted of 14 people: 10 male and 4 female from the age of 11-73[3]. The sample group of hypersensitive bladder and primary detrusor instability participants consisted of 11 people: 3 male and 8 female from the age of 30-80[4] (Table 1A & 1B).

All the participants had received other types of treatment prior to the present capsaicin treatment study, but were not pleased with the results. Some patients suffered from medication side effects, such as dry mouth, noxious, headache, blurred vision and constipation, etc. Information on capsaicin was clearly communicated to everyone before they agreed to participate. All participants received the urodynamic test using the cystometry method (Dantec Manuet machine) that used median filled rate/liquid cystometry program 1 month before and after the capsaicin was instilled in their bladders.

Capsaicin production process :



Evaluation process

1. Clinical: Each patient kept a record of his or her voiding/day in a chart form. This chart was used to record the time of micturition, volume, any episodes of urgency, and incontinence.

2. Urodynamic: Measurements of flow rates, pattern, detrusor pressure, intravesical pressure, abdominal pressure, and maximum cystometric bladder capacity.

Table 1A. Overactive bladder patients.

Number	Age	Sex	Diagnosis
1	11	F	DH
2	27	M	DH
3	32	M	DH
4	22	M	DH
5	70	F	DI
6	15	M	DH
7	20	M	DH
8	63	F	DI
9	23	M	DH
10	59	M	DH
11	29	M	DH
12	21	M	DH
13	69	F	DH
14	73	M	DI

DH = Detrusor hyperreflexia
DI = Detrusor instability

Table 1B. Hypersensitive bladder & detrusor instability patients.

Number	Age	Sex	Diagnosis
1	72	M	DI
2	60	M	DI
3	68	F	DI
4	61	F	DI
5	43	F	HB
6	68	F	DI
7	50	F	DI
8	69	M	HB
9	30	F	HB
10	62	F	HB
11	80	F	DI

DI = Detrusor instability
HB = Hypersensitive bladder

Table 2A. Capsaicin results in overactive bladder.

Parameter	Pre-capsaicin instillation	Post-capsaicin instillation	P-value	% improved	%
Frequency	16.5 ± 4.8	8.6 ± 2.5	< 0.01	12/13	92
Leakage	9.7 ± 8.1	2.4 ± 4.3	< 0.01	9/9	100
Pad needed	2	0	-	2/2	100
Bladder capacity (ml)	160.1 ± 123.3	236.9 ± 146.1	< 0.02		

Table 2B. Capsaicin results in hypersensitive bladder & primary detrusor instability.

Parameter	Pre-capsaicin instillation	Post-capsaicin instillation	P-value
Frequency (day : night)	19.45 ± 17.99:7.09 ± 6.30	12.00 ± 8.91:4.09 ± 3.08	< 0.05
Bladder capacity (ml)	197.0 ± 156.06	323.45 ± 129.46	< 0.009

Intravesical instillation process

1. The patient lay down flat.
2. A urine tube (#16F) was inserted.
3. The bladder was filled with 2 per cent xylocaine without adrenaline, approximately half of the bladder capacity. The solution was kept inside the bladder for 15 minutes.
4. The bladder was filled with capsaicin, approximately half of the bladder capacity for 30 minutes.
5. For those patients who could not bear the pain, another alternative was to use regional or general anesthesia.

RESULTS

1. Clinical results

Symptoms were clinically improved and were statistically significant (Table 2A & 2B).

2. Urodynamic results

Bladder capacity improved and was statistically significantly (Table 2A & 2B) and detrusor pressure was significantly reduced in overactive bladders, but not in primary detrusor instability and hypersensitive bladder patients. (Table 3A & 3B)

Side effects

1. Burning sensation around the genital area and sweating while being treated with capsaicin. The

Table 3A. Capsaicin results in overactive bladder.

Parameter	Pre-capsaicin instillation	Post-capsaicin instillation	P-value
Pmcc	71.1 ± 29.2	57.3 ± 27.2	< 0.03
Pvoid	74.8 ± 35.3	65.1 ± 35.0	< 0.32

Pmcc = detrusor pressure at maximum cystometry capacity (Cm H_2O)
Pvoid = Voiding pressure (Cm H_2O)

Table 3B. Capsaicin results in hypersensitive bladder and primary detrusor instability.

Parameter	Pre-capsaicin instillation	Post-capsaicin instillation	P-value
Pmcc	32.64 ± 22.77	36.64 ± 19.22	< 0.823
Pvoid	47.10 ± 20.35	48.10 ± 21.11	< 0.959

Pmcc = detrusor pressure at maximum cystometry capacity (Cm H_2O)
Pvoid = Voiding pressure (Cm H_2O)

Table 4. Previous reports from many authors.

Authors	No. of patients	Dose (mM/L)	Symptomatic improvement	%	Urodynamic improvement	%	Maximum duration effect (mths)
Fowler[11]	14	1-2	9/14	64	10/14	71	6
Geirsson[12]	10	2	4/10	40	9/10	90	7
Igawa[13]	5	1-2	5/5	100	5/5	100	6
Cruz[14]	16	1	14/16	100	13/16	81	/
deRidder[15]	30	1-2	14/18	100	-	-	-
Viroj	14	1	12/13	92	9/14	64	-

burning sensation did subside after capsaicin was flushed out from the bladder. In some cases, this sensation lasted up to 1 week.

2. The first 2 weeks after the treatment, some patients experienced frequent urination. However, the patients usually felt better in the 3rd week: had less leakage, less urgency, etc.

3. Urinated with blood: 2 cases from each study group. [2 of 14 (overactive bladder) and 2 out of 11 (hypersensitive bladder and primary detrusor instability) participants.]

Comments

A overactive or hypersensitive bladder[1, 5], both intrude on the patient's physical and mental health. Overactive and hypersensitive bladder symptoms prevent patients from living their lives normally, because these symptoms are beyond their control. They are unable to carry out their regular daily routines as they wish. The major factors that affect these patients are categorized into three areas: mental, social, and economical. These uncontrollable symptoms cause extreme stress to the patients' bodies and minds.

The diagnosis of an overactive bladder may be divided into those with a detrusor instability and those with detrusor hyperreflexia. Detrusor hyperreflexia is defined as overactivity due to disturbance of nervous control mechanisms such as a cerebrovascular accident or suprasacral cord injury. The detrusor instability or unstable detrusor can be caused by bladder outlet obstruction (BOO) such as benign prostatic hypertrophy in males and external meatal stenosis in females, or be idiopathic (primary detrusor instability) in origin[6]. The term "overactive bladder" may be used when the diagnosis is made on the basis

of symptoms, and the term "detrusor overactivity" may be reserved for a diagnosis based on urodynamics.

Frequent urination is defined as urination more than 8 times in 24 hours, urgency is defined as a strong desire to void, and urge incontinence is defined as the involuntary flow of urine associated with urgency. The clinical conditions associated with these symptoms are termed motor urgency and motor urge incontinence. Sensory urgency or sensory urge incontinence are terms used when these symptoms are present but there are no involuntary detrusor contractions on filling cystometry (hypersensitive bladder).

At the outpatient Urology Clinic at Siriraj Hospital, about 3-4 female patients and 2-3 male patients present with symptoms of an overactive bladder each day. About 1,300-1,820 patients per year having symptoms of an overactive bladder present to the Division of Urology.

The incidence of overactive bladder between the ages of 20 and 60 years has been estimated at 10 per cent in the asymptomatic elderly (Turner and Warwick, 1979)[7], an overactive bladder is common, occuring in 50 per cent of men over 70 years and in 30 per cent of women of a similar age (Abrams, 1984) [8]. In the symptomatic elderly over 75 years, the incidence is 80 per cent in women and 90 per cent in men (Malone-lee, 1988)[9].

Treatment of an overactive or hypersensitive bladder can be done conservatively by[1]:

1. Bladder retraining or bladder drill.
2. Biofeedback.
3. Pelvic floor exercise.
4. Electrical stimulation.

These treatments do not show impressive results. There are other forms of treatment, such as hypnotherapy and acupuncture. However, these alternatives have failed universal acceptance.

Pharmacotherapy[10]

Various drugs are currently available for the alleviation of an overactive bladder. The majority have antimuscarinic activity and produce inevitable unwanted effects which the clinician must balance against any perceived benefit.

The available drugs are as follows: anticholinergic agents (antimuscarinic), musculotropic relaxants, calcium antagonists, potassium channel openers, prostaglandin inhibitors, β-adrenergic agonists, tricyclic antidepressants, estrogens, etc.

Intravesical instillation[3,4,11-17]

Intravesical instillation of drugs are available such as capsaicin, Resiniferatoxin and Oxybutynin. In Thailand intravesical instillation with capsaicin is available at Siriraj Hospital and has been reported by Viroj et al (1999) and Banjerd et al (2001) with good results.

These are specific neurotoxins that desensitise C-fibre afferent neurones which may be responsible for signals that trigger detrusor instability. Resiniferatoxin is 1,000 times more potent than capsaicin, but with minimal initial excitatory actions.

Based on the focus group study, patients suffered less overactive and hypersensitive bladder symptoms after receiving capsaicin treatment. They experienced less urgency, frequency, and more bladder capacity. Most of these patients no longer had to depend on antimuscarinic medication.

Capsaicin is extracted from chili. which is abundant in Thailand and inexpensive to obtain. It can be easily produced, and has been broadly used in medical history for more than 120 years, for decreasing various noxious stimuli in postherpetic neuralgia and vasomotor rhinitis patients.

SUMMARY

Overall, capsaicin treatment is recommended as another good alternative to overactive and hypersensitive bladder cure. Capsaicin can be obtained in Thailand from an abundant, natural resource, chili. Based on the present study, capsaicin provided great improvement results for patients who had suffered from overactive and hypersensitive bladder symptoms, with no long-term major side effects[18]. It is also inexpensive and can be easily produced, thus the treatment process is very economical.

(Received for publication on February 28, 2003)

REFERENCES

1. Abrams PH, Blaivas JG, Stanton SL, Andersen JT. Standardization of terminology of lower urinary tract function. Neurourol Urodyn 1988; 7: 403-27.
2. Dasgupta P, Fowler CJ. Chillies : From antique to urology. Brit Urol 1997; 80: 845.
3. Wein AJ. Pharmacology of incontinence. Urologic Clin North Amer 1995; 7: 403.
4. Yoshimura N, Erdman SL, Snider NW, de Groat WC. Effects of spinal cord injury on neurofilament immunoreactivity and capsaicin sensitivity bladder. Neuroscience 1998; 83: 633.
5. Abrams PH, Bliavas JG, Stanson SI, Anderson JT. Standardization of lower urinary tract function. Neurological Urodynamics 1998; 7: 403.
6. De Seze M, Wiart L, Ferrie're JM, et al. Intravesical Instillation of capsaicin in Urology : A Review of the Literature. Eur Urol 1999; 36: 267-77.
7. Tuner-Warwick R. Observative on the function and dysfunction of the sphincter and detrusor mechanisms. Urol Clin North Am 1979; 6: 23-9.
8. Abrams PH. Bladder instability: Concept, clinical associations and treatment. Scand J Urol Nephrol 1984; 87 (Suppl): 7-13.
9. Malone-Lee JG. New data on urodynamics in the symptomatic elderly. Neurourol Urodyn 1988; 7: 119-222.
10. Wein AJ. Pharmacology of incontinence. Urologic Clin North Amer 1995; 22: 557.
11. Fowler CJ, Jewkes D, McDanard WJ, et al. Intravesical capsaicin for neurogenic bladder dysfunction. Lancet 1992; 339: 1239.
12. Geirsson G, Fall M, Sulivan L. Clinical and urodynamic effects of intravesical capsaicin treatment in patients with chronic traumatic spinal cord detrusor hyperreflexia. J Urol 1995; 154: 1825.
13. Igawa Y, Koniyama I, Nishizawa S, Ogawa A. Intravesical capsaicin for treatment of autonomic dysreflexia in patients with spinal cord injury. J Urol 1996; 155: 591.
14. Cruz F, Guinaraes M, Silva C, et al. Desensitization of bladder sensory fibers by intravesical capsaicin has long lasting clinical and urodynamic effects in patients with hyperactive or hypersensitive bladder dysfunction. J Urol 1997; 157: 585.
15. deRidder D, Chanceller MB, Watanabe T, et al. Intravesical capsaicin as a treatment for refractory detrusor hyperreflexia : A dual center study with long-term follow-up. J Urol 1997; 158: L2087.
16. Chancellor MB, de Groat WC. Intravesical capsaicin and Resiniferatoxin therapy : Spicing up the ways to treat the overactive bladder. J Urol 1999; 162: 3.
17. Craft RM, Cohen SM, Porreca F. Long lasting desensitization of bladder afferents following intravesical resiniferatoxin and capsaicin in the rat. Pain 1995; 61: 317.
18. Dasgupta P, Chandiramani V, Parkinson MC, et al. Treating the human bladder with capsaicin : Is it safe? European Urology 1998; 33: 28.

ประสิทธิภาพของ แคพไซซิน ไทย ในการรักษาภาวะกระเพาะปัสสาวะบีบตัวไวเกินและกระเพาะปัสสาวะรับรู้ไวเกิน

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เป็นผลการวิจัยการใช้ แคพไซซิน ในการรักษาภาวะกระเพาะปัสสาวะบีบตัวไวเกินและภาวะกระเพาะปัสสาวะรับรู้ไวเกิน เป็นการวิจัย 2 ชุด ชุดแรก ในผู้ป่วยที่มีกระเพาะปัสสาวะบีบตัวไวเกิน 14 คน ชุดที่ 2 เป็นภาวะกระเพาะปัสสาวะรับรู้ไวเกินและภาวะกระเพาะปัสสาวะบีบตัวไวเกินโดยไม่รู้สาเหตุ ทั้ง 2 ชุด ได้รับการใส่ แคพไซซิน เข้ากระเพาะปัสสาวะ สารละลายประกอบด้วย แคพไซซิน ความเข้มข้น 1 มิลลิโมล/ลิตร ละลายใน 30% เอธานอล 100 มิลลิลิตร ผู้ป่วยทุกคนต้องได้รับการตรวจทางยูโรพลศาสตร์ 1 เดือน ก่อนและหลังการได้รับใส่สารละลาย แคพไซซิน เข้ากระเพาะปัสสาวะ

ผลการรักษาในทั้งภาวะกระเพาะปัสสาวะบีบตัวไวเกินและความรู้สึกไวเกินได้ผลดี โดยเฉลี่ยในชุดแรกพบว่า

ความถี่ในการถ่ายปัสสาวะลดลง คือ จาก 16.5 ± 4.8 ครั้ง/วัน เหลือ 8.6 ± 2.5 ครั้ง/วัน

ภาวะปัสสาวะราด จาก 9.7 ± 8.1 ครั้ง/วัน เหลือ 2.4 ± 4.3 ครั้ง/วัน

ความจุของกระเพาะปัสสาวะเพิ่ม จาก 160.1 ± 123.3 มิลลิลิตร เป็น 236.9 ± 146.1 มิลลิลิตร

และแรงบีบตัวของกระเพาะปัสสาวะลดลง จาก 71.1 ± 29.2 เซนติเมตรน้ำ เหลือ 57.3 ± 27.2 เซนติเมตรน้ำ

และในภาวะกระเพาะปัสสาวะรับรู้ไวเกินและบีบตัวไวเกิน ในชุดที่ 2

ความถี่ในการปัสสาวะ (จำนวนครั้ง) ลดจากกลางวันต่อกลางคืน = 19.45 ± 17.99 : 12.00 ± 8.91 เหลือ 7.09 ± 6.03 : 4.09 ± 3.8

ความจุกระเพาะปัสสาวะเพิ่มจาก 197.0 ± 156.06 มิลลิลิตร เป็น 323.45 ± 129.46 มิลลิลิตร

และแรงบีบตัวจากกระเพาะปัสสาวะจาก 32.64 ± 22.77 เซนติเมตรน้ำ เป็น 36.64 ± 19.22 เซนติเมตรน้ำ

ประสิทธิภาพของ แคพไซซิน ต่อภาวะกระเพาะปัสสาวะบีบตัวไวเกินและรู้สึกไวเกินได้ผลดีอย่างน่าพอใจ

ในประเทศไทย เราสามารถสกัด แคพไซซิน จากพริกที่มีอยู่อย่างมากมายในธรรมชาติ ราคาก็ถูก เมื่อพิจารณาถึงประสิทธิภาพและราคาของพริกแล้ว ก็คิดว่าการรักษาโดยวิธีนี้เป็นทางเลือกที่ดี สำหรับภาวะกระเพาะปัสสาวะบีบตัวไวเกินและรู้สึกไวเกิน

คำสำคัญ : แคพไซซิน, กระเพาะปัสสาวะบีบตัวไวเกิน, กระเพาะปัสสาวะรับรู้ไวเกิน

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