

ฉบับนี้ต้นฉบับ



การศึกษาประสิทธิภาพของการใส่สาร capsaicin ในกระเพาะปัสสาวะในกลุ่มอาการปวดอุ้งเชิงกรานเรื้อรังและภาวะปวดกระเพาะปัสสาวะ

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บทคัดย่อ

วัตถุประสงค์: เพื่อศึกษาประสิทธิภาพของ capsaicin ในการรักษาอาการปวดและการบรรเทาอาการปัสสาวะบ่อยของกลุ่มอาการปวดอุ้งเชิงกรานเรื้อรังและภาวะปวดกระเพาะปัสสาวะ

วัตถุประสงค์และวิธีการ: ผู้ป่วยที่ได้รับการวินิจฉัยว่าเป็นกลุ่มอาการปวดอุ้งเชิงกรานเรื้อรังและภาวะปวดกระเพาะปัสสาวะ (chronic pelvic pain syndrome and painful bladder syndrome) ที่รับการรักษาที่โรงพยาบาลศิริราช จำนวน 19 คน ตั้งแต่กรกฎาคม 2550-มกราคม 2552 ได้รับการรักษาโดยใส่สาร capsaicin 1 mM/L ใน 30% ethanol 100 cc ในกระเพาะปัสสาวะ (intravesical capsaicin instillation) ภายใต้การให้ยาชาเฉพาะที่ Local (Intravesical Xylocaine) หรือภายใต้การบริหารยาชาเฉพาะที่เข้าเส้นประสาทไขสันหลัง (spinal block) และประเมินอาการปวด (pain score) และบันทึกความถี่ของการปัสสาวะก่อนใส่สาร capsaicin เปรียบเทียบกับหลังใส่สาร capsaicin 2 สัปดาห์, 1, 2 และ 3 เดือนตามลำดับ การศึกษาเป็นแบบ prospective experimental study

ผลการศึกษา: ผู้ป่วยทั้งหมด 19 คน เป็นเพศหญิงจำนวน 12 คน เพศชาย 7 คน อายุเฉลี่ย 47 ปี มีระยะเวลาการดำเนินโรคเฉลี่ย 3.5 ปี มีโรคประจำตัวเป็นเบาหวาน 11% (2/19) ความดันโลหิตสูง 11% (2/19) ประวัติติดเชื้อทางเดินปัสสาวะ 21%(4/19) ประวัติผ่าตัดบริเวณอุ้งเชิงกราน 26%(5/19) ประวัติการรักษาด้วยยา 78%(15/19) ประวัติรักษาโดยการใส่สาร capsaicin 21%(4/19) คะแนนการปวดโดยเฉลี่ย (Average pain score) 7.5 ± 1.7 (median \pm SD) ปัสสาวะเวลากลางวันเฉลี่ย 10 ± 3.8 ครั้ง ปัสสาวะเวลากลางคืนเฉลี่ย 4.5 ± 2.9 ครั้ง ผลการศึกษาเปรียบเทียบ pain score ก่อนและหลังใส่สาร capsaicin พบว่าอาการปวด (pain score) ลดลงจาก 7.5 ± 1.7 ก่อนใส่สาร capsaicin เป็น 5 ± 2.3 , 2.5 ± 2.4 , 3 ± 2.9 , 3 ± 2.6 หลังใส่สาร capsaicin ที่ 2 สัปดาห์ 1, 2 และ 3 เดือนตามลำดับ มีความแตกต่างอย่างมีนัยสำคัญทางสถิติ ($p < 0.01$) และความถี่ในการปัสสาวะทั้งเวลากลางวันและกลางคืนลดลงอย่างมีนัยสำคัญทางสถิติ ยกเว้นช่วง 2 สัปดาห์แรกหลังใส่สาร capsaicin เนื่องจากมีอาการระคายเคืองกระเพาะปัสสาวะซึ่งเป็นผลจากสาร capsaicin

สรุป: การใส่สาร capsaicin ในกระเพาะปัสสาวะสามารถลดอาการปวดในกลุ่มอาการปวดอุ้งเชิงกรานเรื้อรังและภาวะปวดกระเพาะปัสสาวะได้อย่างมีนัยสำคัญทางสถิติ ($p\text{-value} < 0.01$) และสามารถลดอาการปัสสาวะบ่อยได้

Efficacy of intravesical capsaicin in chronic pelvic pain syndrome and painful bladder syndrome.

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Abstract

Purpose: To study efficacy of intravesical capsaicin in chronic pelvic pain syndrome and painful bladder syndrome.

Materials and Methods: This study was prospective experimental study. All 19 patients in outpatient clinic were diagnosed chronic pelvic pain syndrome or painful bladder syndrome. We recorded from July 2007 to January 2009 at Siriraj Hospital. These patients were performed intravesical capsaicin instillation with 1 mM/L in 30% ethanol in normal saline 100 cc under spinal block or local intravesical 2% Xylocaine instillation. Pain score, daytime urination, nighttime urination were recorded before and after procedure 2 weeks, 1, 2 and 3 months.

Results: In 19 patients, there were 12 female (68.2 %) and 7 male (36.8 %) mean age was 47 years. Average duration of disease was 3.5 years. Average pain score (median \pm SD) was 7.5 \pm 1.7 (median \pm SD) and Daytime urination was 10 \pm 3.8 times and Nighttime urination was 4.5 \pm 2.9 times. A significant decrease in pain score was found from 7.5 \pm 1.7 pretreatment to 5 \pm 2.3, 2.5 \pm 2.4, 3 \pm 2.9, 3 \pm 2.6 at 2 weeks 1, 2 and 3 months after treatment (p-value<0.01). The frequency of urination was significant decrease both daytime and nighttime urination except first 2 weeks after intravesical capsaicin instillation because there was irritative symptoms from side effect of capsaicin.

Conclusions: Intravesical capsaicin instillation was provided good results and safe for chronic pelvic pain syndrome and painful bladder syndrome. There was significant decrease pain score and frequency of urination. But side effect of capsaicin was found in first 2 weeks due to irritative symptoms.

Key words: Chronic pelvic pain syndrome, Painful bladder syndrome, Pain score, Capsaicin

Chronic pelvic pain syndrome and Painful bladder syndrome were syndrome of pain and some patients have frequency of urination. In out patient clinic of urologic division was found incidence of these disease 5-11[1]%. And there was some patients came to other clinics such as Gynecology, Medicine, Psychiatry and General practitioner. Pain with or without frequency of urination were common symptoms to complaint with us. These symptoms were bothering them and poor quality of life. There was multifactorial factors that caused the symptoms. So, there were many treatments such as medication (pain killer, muscle relaxant, antibiotic, anticholinergic, antihistamine, β -blocker), Intravesical therapy (DMSO, Resiniferatoxin, Anti histamine, Silver nitrate, doxorubicin, Botulinum toxin, Capsaicin), Neuromodulator and finally Bladder augmentation.

Capsaicin, a substance that is extracted from chili, the action passes to vallinoid receptor type I in bladder and controls C-fiber as neurotoxin. Lazzeri M, et al[2] reported the clinical beneficial effect of capsaicin in patients. Pain is decreased by capsaicin treatment. Stimulation of C-fiber by Vallinoid receptor and mediators is one of those mechanisms of pain sensation. Capsaicin is one substance that reduces pain. In Thailand, Capsaicin is extracted from *Capsicum frutescens* by Siriraj Hospital, Mahidol university. Capsaicin 1 mM/L in 30% ethanol 100 cc is prepared with sterile technique. de Seze, et al[3] studied by intravesical capsaicin instillation in 200 patients's bladders. He found that all patients were safe and there were no cellular changes.

In this study, we want to study that intravesical capsaicin instillation can reduce pain and decrease frequency of urination in chronic pelvic pain syndrome and painful bladder syndrome.

Objective

To study efficacy of intravesical capsaicin

instillation in chronic pelvic pain syndrome and painful bladder syndrome. Primary outcome was pain score and secondary outcome was frequency of urination.

Materials and Methods

This research was approved by the ethics committee of Siriraj hospital, Mahidol University and all patients signed to the consents before treatment. The study design was prospective experimental study. We collected data between July 2007 to January 2009. The patients who were diagnosed chronic pelvic pain syndrome or painful bladder syndrome would follow inclusion criterias: symptoms more than 6 months, age over 18 years, urination by themselves and commitment to follow up for 3 months. All of patients signed the consent form before treatment. For the exclusion criterias: the patients had pathologic disease that can explain the symptoms eg. bladder tumor, vesical calculi, UTI, contracted bladder, neuropathic bladder, bladder outlet obstruction, post radiation effect.

We studied 19 patients; 12 women and 7 men with chronic pelvic pain syndrome and painful bladder syndrome. All patients were performed history taking and physical examination especially genitalia and digital rectal examination. The woman had gynecological check up. Pain score and voiding chart was recorded before treatment. Pain score was 0 to 10. Average pain score, worst pain score and least pain score were recorded before treatment. Voiding chart was recorded. Further proper investigations were checked such as urine analysis, urine culture, PSA level for men (age >50 years old), cystoscopy, cystometry, uroflowmetry, residual urine before treatment. The patients's data was collected and personalised.

Procedure: Foley catheter 16 Fr. was indwelled. Capsaicin 1 mM/L in 30% ethanol in normal saline 100 cc was filled into bladder for 30 minutes and

then normal saline was irrigated. Capsaicin instillation was done under spinal block or under local (intravesical 2% Xylocaine solution 30 cc for 30 minutes, Fentanyl 1 ml i.v., Arcoxia 120 mg oral for 30 minutes before capsaicin instillation). Catheter was removed immediately after capsaicin instillation in patients with local anesthesia but the patients with regional anesthesia was removed next day after capsaicin instillation under spinal block. Pain score,

daytime urination, nighttime urination was recorded 2 weeks, 1, 2 and 3 months after capsaicin instillation.

Statistics analysis

Pain score was shift to the right distribution curve. So nonparametric statistic was used to compare the different outcomes. (Friedman test and Wilcoxon's Signed-Rank test)

Results

Primary data of all patients were following.

	N (%)	Median±SD (Min, Max)
Sex		
Men	7 (36.8)	
Women	12 (63.2)	
Age (Year)		47.0±13.8 (25,73)
Underlying disease		
Diabetes millitus	2 (10.5)	
Hypertension	2 (10.5)	
History of UTI	4 (21.1)	
History of Pelvic surgery	8 (42.1)	
Duration of disease		3.5±3.3 (0.5,10)
Previous treatment		
Medication	15 (78.9)	
Intravesical capsaicin instillation	4 (21.1)	
Area of pain		
Pelvic pain	11 (57.9)	
Scrotal pain	2 (10.5)	
Urethral pain	6 (31.6)	
Pain score		
Worst pain score		8±1.6
Least pain score		5.5±1.7
Average pain score		7.5±1.7
Anesthesia		
Local (Intravesical Xylocaine)	8 (42.1)	
Spinal block	11 (57.9)	

We studied 12 women (63.2%) and 7 men (36.8%). Mean age was 47 years old. Underlying disease was diabetes mellitus and hypertension 11% (2/19). History of UTI 21% (4/19), pelvic surgery 42% (8/19), coffee consumption 16% (3/19). All patients did not have history of trauma, radiation therapy,

alcohol drinking and smoking. Most of them had pelvic pain 57.9% (11/19), urethral pain 31.6% (6/19) and scrotal pain 10.5% (2/19). Average pain score was 7.5 ± 1.7 (Median \pm SD) and daytime urination was 10 ± 3.8 and nighttime urination was 4.5 ± 2.9 . Pain score showed in figure 1.

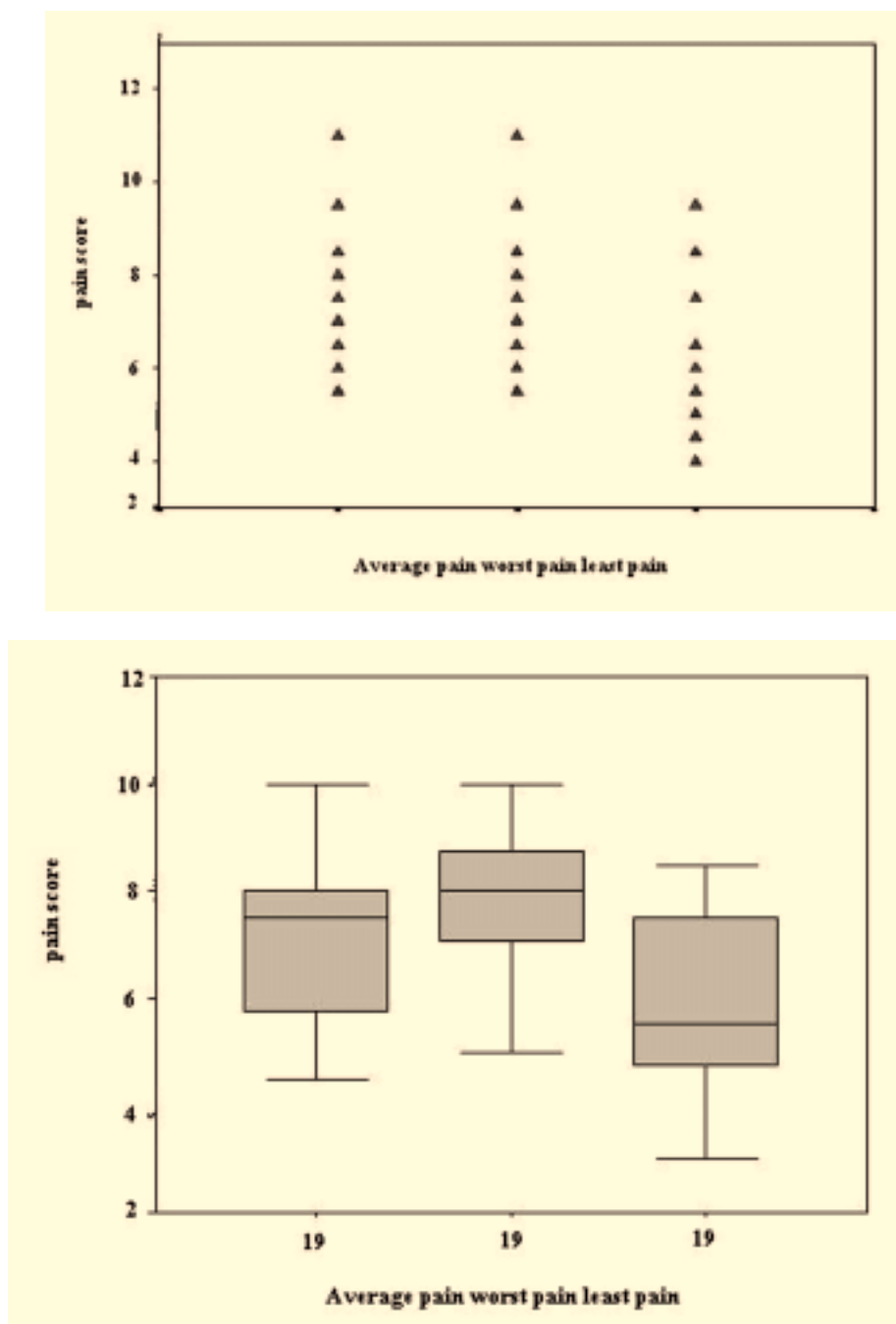


Figure 1 Dot plot and Box plot of Average pain score, Worst pain score, Least pain score

Pain score was decreased from 7.5 ± 1.7 (Median \pm SD) before intravesical capsaicin to 5 ± 2.3 , 2.5 ± 2.4 , 3 ± 2.9 , 3 ± 2.6 at 2 weeks, 1, 2 and 3 months after intravesical capsaicin instillation. It's significant decreased pain score comparing before and after by Friedman test and Wilcoxon's Signed Rank test (p -value <0.01) as table 1 and figure 2.

Daytime urination was decreased from 10 ± 3.8 (Median \pm SD) times before intravesical capsaicin instillation to 7.5 ± 2.6 , 4.5 ± 2.4 , 4.5 ± 2.8 , 4.5 ± 2.8 times at 2 weeks 1, 2 and 3 months after intravesical capsaicin instillation as table 2 and figure 3. The significant decreased daytime urination was found at 1, 2 and 3 months after intravesical capsaicin

Table 1 Pain score pre and post intravesical capsaicin instillation

Pain score	Median \pm SD	Median	Mean	Min, Max	p-value [#]
Pre* intravesical Capsaicin	7.5 ± 1.7	7.5	7.5	0.5,10	
post** 2 weeks	5.0 ± 2.3	5.0	4.1	0,7.5	<0.01
post 1 month	2.5 ± 2.4	2.5	3.2	0,10	<0.01
post 2 month	3.0 ± 2.9	3.0	3.7	0,10	<0.01
post 3 month	3.0 ± 2.6	3.0	3.5	0,10	<0.01

Friedman test

* before intravesical capsaicin instillation

**after intravesical capsaicin instillation

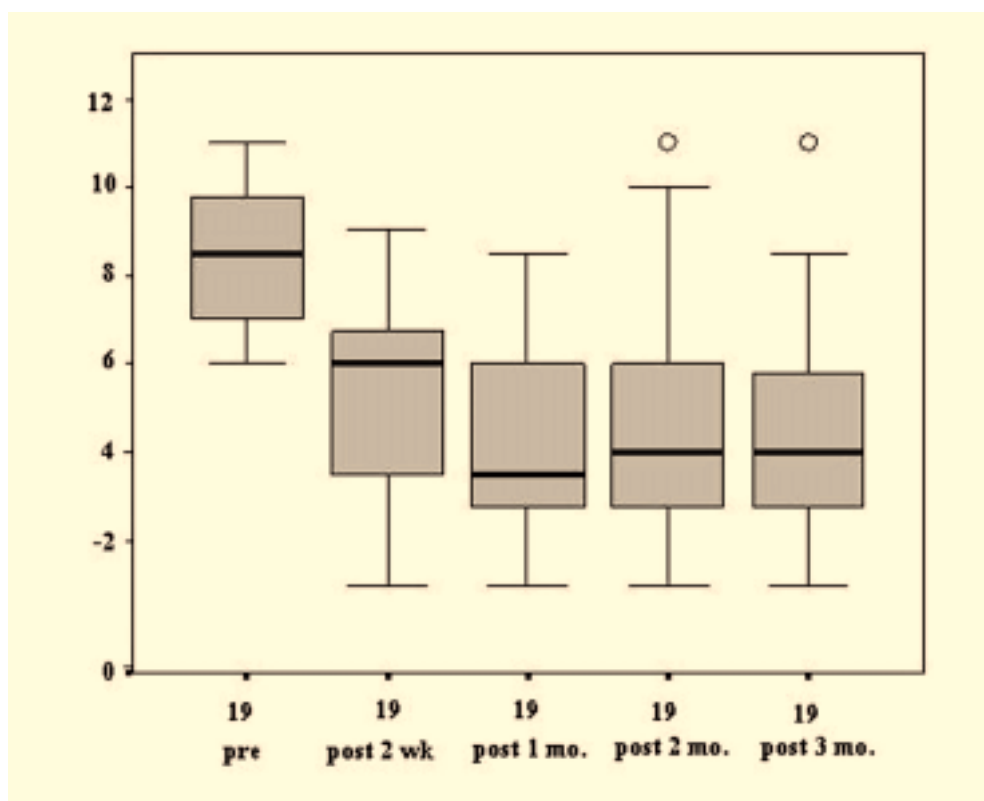


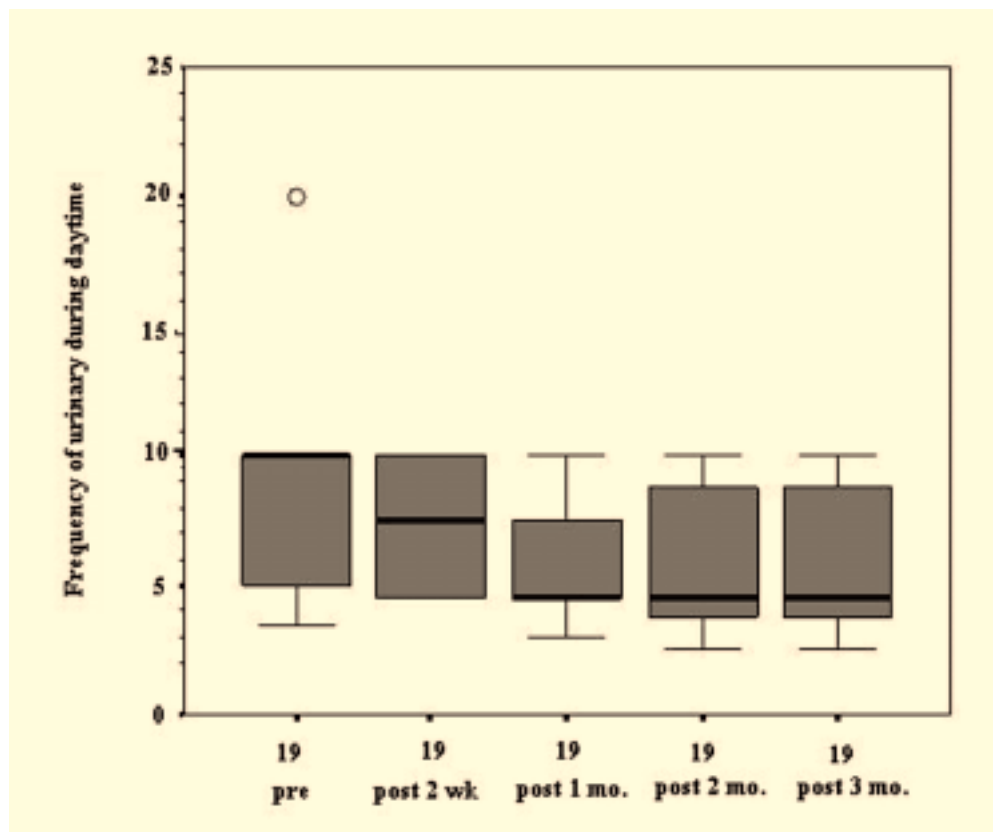
Figure 2 Box plot of pain score after intravesical capsaicin instillation

Table 2 Daytime urination pre and post intravesical capsaicin instillation

Daytime urination	Median \pm SD	Median	Mean	Min, Max
Pre* Capsaicin	10 \pm 3.8	10	8.3	3.5, 20
Post** 2 weeks	7.5 \pm 2.6	7.5	7.3	4.5, 10
Post 1 month	4.5 \pm 2.4	4.5	6.0	3.0, 10
Post 2 month	4.5 \pm 2.8	4.5	6.0	2.5, 10
Post 3 month	4.5 \pm 2.8	4.5	6.0	2.5, 10

* before intravesical capsaicin instillation

**after intravesical capsaicin instillation

**Figure 3** Box plot daytime urination of intravesical capsaicin instillation

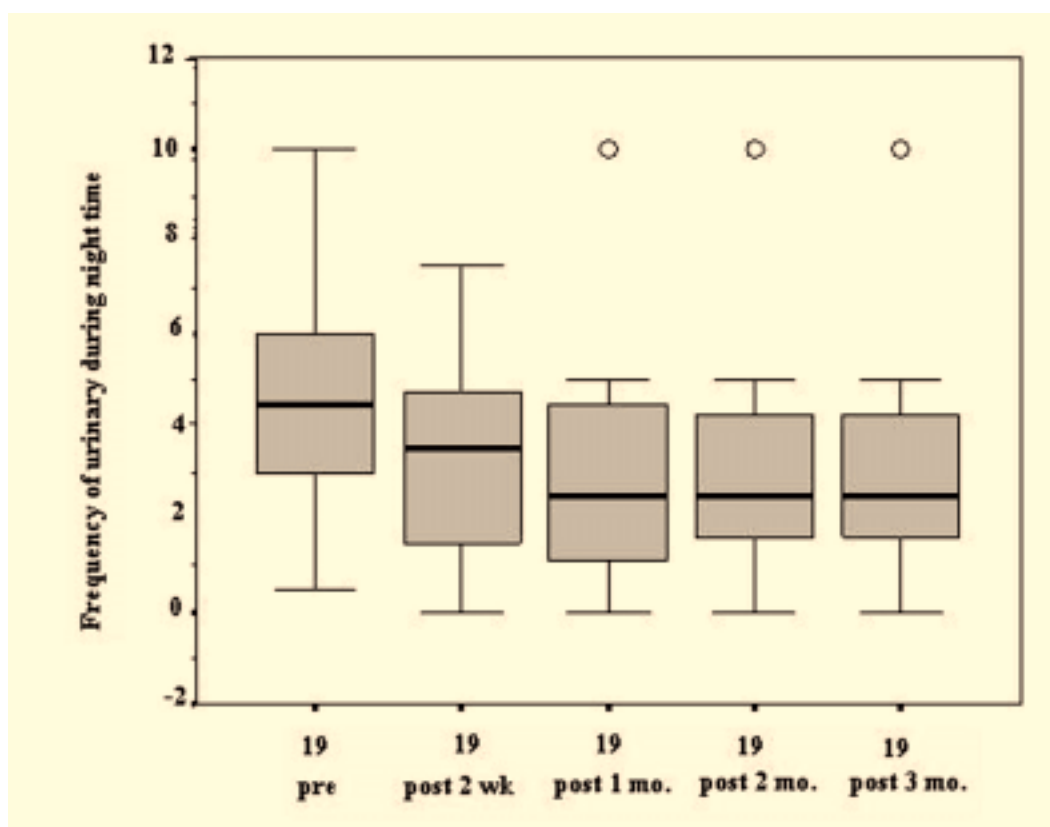
instillation (p- value <0.01) by Friedman test and Wilcoxon's Signed Rank test except first 2 weeks due to bladder irritation from capsaicin as table 4.

Nighttime urination was decreased from 4.5 \pm 2.9

(Median \pm SD) times before intravesical capsaicin instillation to 3.5 \pm 2.2, 2.5 \pm 2.3, 2.5 \pm 2.3, 2.5 \pm 2.3 times at 2 weeks, 1, 2 and 3 months after intravesical capsaicin instillation as table 3 and figure 4. The

Table 3 Nighttime urination pre and post intravesical capsaicin instillation

Nighttime urination	Median±SD	Median	Mean	Min, Max
Pre* Capsaicin	4.5±2.9	4.5	4.7	0,10
Post** 2 weeks	3.5±2.2	3.5	3.4	0,7.5
Post 1 month	2.5±2.3	2.5	2.9	0,10
Post 2 month	2.5±2.3	2.5	3.0	0,10
Post 3 month	2.5±2.3	2.5	2.9	0,10

**Figure 4** Nighttime urination pre and post intravesical capsaicin instillation

significant decreased nighttime urination was found at 1, 2 and 3 months after intravesical capsaicin instillation (p -value <0.01) by Friedman test and Wilcoxon's Signed Rank test except first 2 weeks due to bladder irritation from capsaicin as figure 4.

Complication

Irritative symptoms due to capsaicin were detected in first 2 weeks. We treated them symptomatically with medications (pain killer, anti-spasmodic drug). 2 patients had retained Foley catheter due to

Table 4 The comparison between pre and post intravesical capsaicin instillation at 2 weeks, 1, 2 and 3 months (p-value)

	p-value#			
	Post 2 wks	Post 1 mo	Post 2 mo	Post 3 mo
Pain score	< 0.01	< 0.01	< 0.01	< 0.01
Daytime urination	0.301	< 0.01	< 0.01	< 0.01
Nighttime urination	0.035	< 0.01	< 0.01	< 0.01

Wilcoxon's signed-rank test

severe pain and the catheter could be removed in 2 weeks and had normal voiding.

Conclusion

Intravesical capsaicin instillation provided good results and safe for chronic pelvic pain syndrome

and painful bladder syndrome. There was significant decrease pain score and frequency of urination. But side effect of capsaicin was found in first 2 weeks due to irritative symptoms could be treated symptomatically.

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