

Complete response to acupuncture therapy in female patients with refractory interstitial cystitis/bladder pain syndrome

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ABSTRACT

Objectives: Interstitial Cystitis/Bladder Pain syndrome (IC/BPS) is a considerable issue in urology and gynecology and unfortunately, the treatment options recommended are not fully efficient. Therefore, in this study we aimed to determine the effectiveness of acupuncture treatment in patients with refractory IC/BPS.

Material and methods: 12 refractory IC/BPS female patients received ten sessions of acupuncture twice a week. The visual analog score (VAS), interstitial cystitis symptom index (ICSI), interstitial cystitis problem index (ICPI), O'Leary-Saint symptom score (OSS), Patient Health Questionnaire (PHQ9), Pelvic pain and urgency & frequency patient symptom scale tests (PUF) and maximum voided volume (MVV) was completed in 1st, 3rd, 6th and 12th months following the treatment.

Results: There was a statistically significant decrease in all of the scores evaluated at first month compared with the baseline. While the change in VAS score in 1, 3, 6 and 12th months were found statistically significant, measurements of ICSI, OSS and PUF scores and MVV values in the 6th and 12th months and ICPI and PHQ scores in the 12th month were not found statistically significant compared to the pre-treatment period. Response to treatment for the first three months after acupuncture application was (100%), but this ratio was measured as 33.3% (4/12) in the sixth month and 16.6% in the 12th month (2/12).

Conclusions: The results of this study suggest that acupuncture appears to be an effective, useful, non-invasive method in IC/BPS patients. It can be used as an appropriate treatment method not only in refractory but also in IC patients since it is rather advantageous compared to other treating agents.

Key words: acupuncture treatment, bladder painful syndrome, interstitial cystitis

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INTRODUCTION

Interstitial cystitis (IC) or bladder painful syndrome (BPS) is defined as a clinical syndrome accompanied by chronic, recurrent suprapubic pain, increase in urination frequency and nocturia complaints increasing with bladder filling. Proven infection or significant other local pathologies are not present in this syndrome. Generally negative cognitive, behavioural, emotional and sexual syndromes and sleep disorders accompany. It is evaluated as one of the sub-types of chronic pelvic pain [1, 2]. The prevalence is estimated as 2.71% in females and 1.21% in males. It is seen 10 times more frequent in females than males. The disease occurs generally

between third and fifth decades [3, 4]. Although the etiology is not completely known, autoimmune mechanisms, previous infections, stress, mast cell activation, neuropathic changes and toxic materials in urine are blamed. Disruption of the barrier and permeability in bladder mucosa due to the defects in glycosaminoglycan (GAG) layer in urothelium and exposure to toxic components of the submucosal tissue plays a role in pathogenesis [1, 3].

Many different methods are used in the treatment. Amitriptyline, antihistaminics, anticholinergics, nonsteroidal anti-inflammatory drugs, cyclosporin A, pentosan polysulphate and similar oral drugs were used but it was not

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possible to demonstrate that these drugs were effective for a long time [1, 5]. In studies with different intravesical GAG replacement treatments (hyaluronic acid, chondroitin sulphate, heparin) aiming the renewal of glycosaminoglycan layer, it was shown that they were successful in removing the pain by 48–71%, increasing bladder capacity and recovery of sexual functions and it was observed that the symptoms were acutely relieved. But a high ratio of recurrence was reported in symptoms [3–7]. It was demonstrated that interventional applications such as bladder dilatation, Botulinum toxin A (BTX-A) application, Electromotive drug administration (EMDA), Hyperbaric oxygen, Neuromodulation application, coagulation and Transurethral resection (TUR) in patients with Hunner ulcer were useful in different levels in the treatment [1]. But in long-term follow-up, it is observed that the symptoms of the patients recur and the complaints reappear in the form of attacks. Also more than 11000 \$ is spent yearly per patient for the medical care of IC/BPS patients in USA. Thus different treatment modalities with longer activity and less cost are required [8].

Acupuncture is an important constituent of traditional Chinese medicine which has been used for over 2500 years. Acupuncture is performed by inserting needles into specific points on the skin and its effect depends on 'Qi' which may be defined as vital energy flows in channels called meridians in the body. With acupuncture treatment, the aim is to provide the body balance by removing the energy flow blockage or interruption occurring in these channels and thereby relieving most illnesses including pain. It is stated that acupuncture application increases serotonin, beta endorphin and enkephalin levels which are endogenous opioids in the plasma and brain tissue [9, 10]. Increase in endogen opioids in plasma and brain tissue cause analgesia, sedation, motor functions recovery and immunomodulation. It is stated that this situation has effects on providing pain control of the individual, causing him/her to feel good, be happy, have normal level of appetite and sexual drives and providing psychomotor balance [9, 10]. As it is known, interstitial cystitis is one of the subtypes of chronic pelvic pain that negative cognitive, behavioural, emotional and sexual symptoms accompany. The efficiency of acupuncture in the recovery of functional disorders such as chronic pelvic pain [11, 12], dysuria induced by benign prostate hyperplasia [13] and irritative bladder symptoms [14] were demonstrated in studies. Although use of acupuncture was accepted by urology experts in the previous decade, there is a limited number of studies investigating the efficiency of acupuncture in IC/BPS in literature [15–17]. The aim of this study was to investigate the efficiency of acupuncture in medical treatment resistant IC/BPS female patients.

MATERIAL AND METHODS

Patients who referred to Konya Training and Research Hospital Urology Clinic with symptoms lasting longer than six months such as pelvic pain, feeling of pressure and discomfort and lower urinary system symptoms (nocturia, urgency, frequency and dysuria) between 2012 and 2014 were examined and evaluated due to suspicion for IC/BPS.

IC/BPS diagnosis was excluded in patients who have pathologies such as underlying bladder cancer, urethral diverticulum, spinal cord injury, stroke, Parkinson's disease, multiple sclerosis, spina bifida, cyclophosphamide treatment, radiation treatment to pelvic area, tuberculosis affecting the bladder, uterine cancer, ovarian cancer, vaginal cancer, genital herpes, pregnancy and urinary infection. In order to clarify the diagnosis in the evaluation made for IC/BPS diagnosis, medical story (especially at least one of the symptoms lasting longer than six weeks), physical examination, urinalysis, potassium sensitivity test, hunner, presence of mucosal petechial bleeding and/or glomeration and hunner ulcer with cystoscopy, taking cystology and biopsy from bladder and cystometry/urodynamy application were used [1, 6]. IC/BPS patients who had failed at least 24 weeks of conventional treatments (dietary changes and pelvic exercise with oral pentosanpolysulphate or tricyclic antidepressant, intravesical instillations of heparin, lidocain or hyaluronic acid, applied hydrodistention under anaesthesia) defined as refractory IC/BPS.

Inclusion and exclusion criteria for IC/BPS patients

Inclusion criteria

Refractory IC/BPS patients with visual analog score ≥ 4 , urinating frequency ≥ 8 and negative urinary culture result in the last 30 days, who underwent 10 sessions of acupuncture treatment were included in the study.

Exclusion criteria

Due to the evaluations, patients who had IC/BPS diagnosis but didn't meet inclusion criteria, patients with previous acupuncture treatment, localized skin infections concerning the acupoints, use of anticoagulations and those with bleeding diathesis, completed a total of 10 acupuncture treatment sessions and whose follow-up forms were unreachable were excluded from the study.

A total of 12 volunteers who met inclusion criteria were included in the study.

Intervention

Acupuncture points were determined by an certified acupuncturists based on the Traditional Chinese Medicine (TCM) treatment methods. Acupuncture was per-

formed with sterile, disposable steel acupuncture needles (0.25 mm × 25–40 mm, *Suzhou Kangnian Medical Devices Ltd. Suzhou, PRC*). After the skin was cleaned appropriately with pads containing 70% alcohol, acupuncture needles were applied bilaterally (if appropriate) at SP6, SP9, ST36, LIV3, LI4, KID3, BL33 and CV4 acupoints with a depth of 1–2 cm depending on the anatomical structures below. Acupuncture application points can be seen in Figure 1, Table 1. After

the sense of deqi was taken in patients, needles were left placed at these points for 20–25 minutes. Total 10 sessions of acupuncture treatment was applied to the patients as twice a week for five weeks.

Assessment

The results of O’Leary-Saint symptom score (OSS) (20) consisting of the total of VAS: visual analog score (VAS) (19),

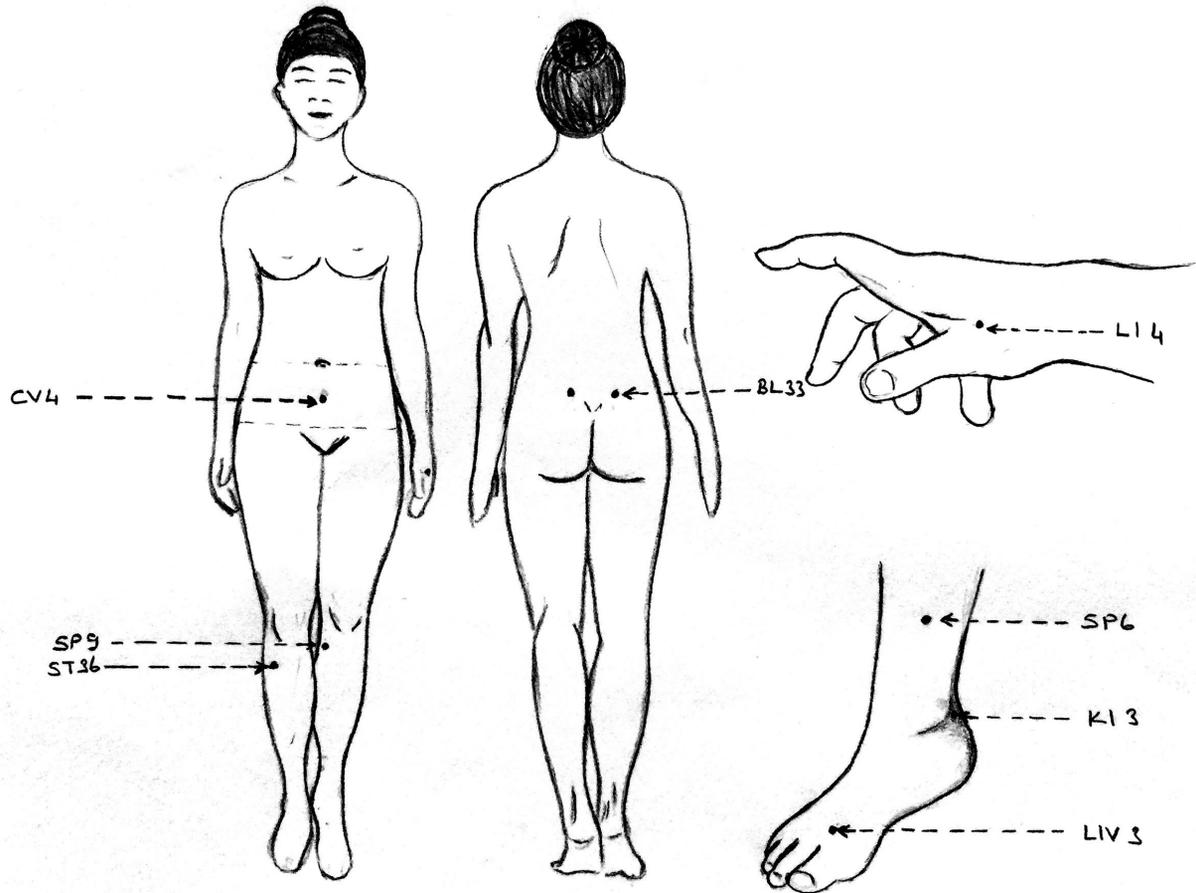


Figure 1. Acupuncture application points

Table 1. Anatomic locations of the acupoints chosen	
Acupoints	Location
SP-6 (Sanyinjiao)	3 tsun above medial malleolus, posterior to the medial border of tibia
SP9 (Yinlingquan)	On the lower border of the medial condyle of the tibia, in the depression between the posterior border of the tibia and gastrocnemius muscle
BL33 (Zhongliao)	On sacrum, in the third posterior sacral foramen
ST36 (Zusanli)	One finger width lateral from the anterior crest of the tibia, in the tibialis anterior muscle
LIV3 (Taichong)	On dorsum of the foot in a depression distal to the junction of the 1 st and 2 nd metatarsal bones
LI4 (Hegu)	On the dorsum of the hand, between the 1 st and 2 nd metacarpal bones
KI3 (Taixi)	In depression midway between the tip of the medial malleolus and the attachment of the Achilles tendon, level with the tip of the medial malleolus
CV-4 (Guanyuan)	On the lower abdomen and on the anterior midline, 3 tsun below the centre of umbilicus

Table 3. Binary statistical analysis of the change in 1, 3, 6, 12th months compared to the pre-treatment values of MVV and all scores (n = 12)

Score	0–1 month p value ⁺	0–3 month p value ⁺	0–6 month p value ⁺	0–12 month p value ⁺
VAS	< 0.001	< 0.001	0.002	0.01
ICSI	0.004	0.009	0.12	0.84
ICPI	0.003	0.004	0.04	0.76
OSS	0.001	0.002	0.053	0.96
PHQ 9	0.006	0.01	0.04	0.3
PUF	0.02	0.04	0.2	0.43
MVV	0.003	0.004	0.08	0.12

⁺Wilcoxon signed-rank test

lower than patients with end stage renal failure who had hemodialysis treatment [23]. Acupuncture is accepted as a scientific treatment method and is commonly used in acute and chronic pain conditions. But there is a limited number of studies supporting the use of acupuncture as an effective treatment option for IC/BPS in literature [16, 17]. Honjo et al. investigated the effect of sacral acupuncture on urinary sensory dysfunction on patients whom had OAB and/or suspected BPS and reported significant decrease in 24-hour frequency and VAS for pain, significant increase in maximum voided volume [24]. Katayama et al investigated the efficiency of acupuncture and moxibustion therapy on 8 patients with refractory IC and reported that there was a significant recovery in the symptoms of three patients [17].

It is considered that acupuncture is effective on IC/BPS symptoms through a few mechanisms. Afferent and efferent innervations of the bladder is formed by sympathetic nerves originating thoracic 11-lumbal 2 (T12-L2) in addition to parasympathetic and somatic nerves originating sacral 2–4 [25]. Parasympathetic system is the primary responsible system in bladder emptying. While the contraction of the bladder is provided by the parasympathetic nervous system through muscarinic receptors, sympathetic nerve system prevents the reflex activity of the detrusor and contributes to the storage of the urine during the bladder filling. The external urethral sphincter is under somatic control. The effect of acupuncture on on urination control and decreasing IC/BPS symptoms (especially urgency and pain) can be explained by inhibition in the sensory afferent nerve of the bladder, parasympathetic nerve system activation and regulation of autonomous nerve system balance [15, 25]. According to the traditional meridian theory, an acupoint has its own therapeutic property due to its specific place and related meridian. Therefore we selected the acupoints corresponding to the segmental innervation of the bladder [26, 27]. BL33 acupoint is on the third sacral nerve root and is associated with parasympathetic nerve segmental innervation. SP6, ST36 and KI3 acupoints are located on

the legs, corresponds to the innervation of skin dermatomes L4-S2 and is considered to assist bladder function by strengthening energy. While SP6 acupuncture point is preferred for urology, gynecology and genital system disorders, KI3 acupuncture point is the best point for urinary output.

Acupuncture is one of the standard neuromodulation therapies. Human brain is closely involved in the control of the micturation. Functional magnetic resonance imaging (MRI) studies demonstrated that there is a significant connection between brain activity and acupuncture treatment [28]. This was confirmed by Hui Wang and et al. in which acupuncture stimulation of the sacral vertebrae affects the neurons in the micturition center [29]. They showed that acupuncture suppressed bladder activity, altered the firing profiles of bladder activity-related neurons in and around Barrington's nucleus via GABAergic system mediating [29]. Similarly Hino et al. reported the result that acupuncture to the sacral periosteum improved acetic acid-induced bladder irritation in rats by inhibiting capsaicine sensitive C-fiber activation [30]. Stimulation sacral S2–S3 vertebrae correspond to the acupoint BL33. In IC/BPS patients, we believed that brain modulation by acupuncture may also play a role in preventing the transmission of pain impulses to the brain over the spinal cord.

Ideal number of sessions and duration of treatment are not clearly established in acupuncture treatment. Thus different applications such as 6, 10 or 12 sessions are seen in studies [11, 16, 17]. Katayama et al. applied acupuncture treatment once a week for three months on 8 refractory IC patients and reported that the treatment was effective in three patients (38%) but efficiency increased when the treatment was repeated [17]. In our study after a total of 10 sessions of acupuncture it was detected that the treatment response was quite good in the first month. In the 6th month, the change in ICSI, OSS and PUF scores and MVV values demonstrated that the efficiency of acupuncture treatment started to lose its efficiency. In the 12th month all score values and MVV values came close to the pre-treatment values. This

study has shown that with the application of 10 acupuncture sessions in refractory IC patients, the patients provided a complete respond for the first three months (100%). We also think that in IC patients, repetition of acupuncture sessions after the third month will increase the efficiency of treatment and recovery time in the symptoms. Without making repetition after application, the respond rate to treatment in the 12th month degraded to 16.6%.

Our study showed that acupuncture treatment has a significant positive effect on bladder volume for the first three months. We think that this situation is parallel to the decrease in pain caused with bladder tension and the scores, increases in the score values occurring after the third month of application affected the urination volume negatively. We think that we may reach more positive results on urination volume with acupuncture treatment supported by bladder hydrotension. We also think that making prospective randomized controlled studies including a group of patients with a higher number of patients, also evaluating repetitive sessions and supported with bladder hydrotension would present the effect of acupuncture better in IC patients.

CONCLUSIONS

Acupuncture treatment is an effective, useful, non-invasive traditional method in IC/BPS patients. We think that it may be safely used even in the first diagnosis period of the disease as an appropriate treatment method not only in refractory but also in all IC patients due to not having a shown side effect and being rather advantageous due to its cost-effectiveness compared to other treating agents. But we also think that planning the treatment in repetitive sessions in appropriate patients would increase the efficiency of the treatment.

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