

Interstitial Cystitis and Endometriosis in Patients With Chronic Pelvic Pain: The “Evil Twins” Syndrome

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ABSTRACT

Objective: To determine the prevalence of interstitial cystitis and endometriosis in patients with chronic pelvic pain.

Methods: A prospective analysis was conducted in 178 women with CPP who presented with bladder base/ anterior vaginal wall and/or uterine tenderness, with or without irritative voiding symptoms. The Potassium Sensitivity Test was used to assess bladder epithelial dysfunction. Patients were evaluated with concurrent laparoscopy and cystoscopy with hydrodistention.

Results: Laparoscopic findings among the 178 patients with chronic pelvic pain supported a diagnosis of endometriosis in 134 (75%) patients, and cystoscopy confirmed a diagnosis of interstitial cystitis in 159 (89%) patients. Both interstitial cystitis and endometriosis were diagnosed in 115 patients (65%). The Potassium Sensitivity Test was positive in 146 (82%) patients, with 140 (96%) of these patients diagnosed with interstitial cystitis and 105 (72%) with endometriosis.

Conclusions: Results of this prospective study show that interstitial cystitis and endometriosis may frequently co-exist in patients with chronic pelvic pain. A positive Potassium Sensitivity Test accurately predicted the presence of interstitial cystitis in 96% of these patients with chronic pelvic pain, as confirmed by cystoscopic hydrodistention. It is necessary to consider the diagnosis of endometriosis and interstitial cystitis concurrently in the evaluation of patients with chronic pelvic pain to avoid unnecessary delay in identifying either condition.

Key Words: Interstitial cystitis, Endometriosis, Chronic pelvic pain.

INTRODUCTION

Chronic pelvic pain (CPP) is estimated to affect more than 9 million women in the United States.¹ Up to 40% of laparoscopies and 10% to 12% of all hysterectomies are performed for CPP.^{2,3} In addition to lost productivity and decreased quality of life, the diagnosis and treatment of CPP consumes nearly \$3 billion of health care expenditures annually.¹

The management of CPP is challenging due to the numerous possible differential diagnoses and contributing factors associated with this condition. Possible differential diagnoses include endometriosis, endosalpingiosis, pelvic adhesions, ovarian remnant syndrome, interstitial cystitis (IC), adenomyosis, and uterine leiomyomas.⁴⁻⁷ These conditions may present with similar symptoms, and one or more may exist concomitantly in a given patient.⁸

Endometriosis is one of the more prevalent gynecologic diagnoses among women with CPP, affecting more than half of those patients who receive a diagnosis for their CPP.^{1,2,5,6,9-11} Symptoms include dyspareunia, cyclic perimenstrual low abdominal pelvic pain, symptom flares after sexual intimacy, and irritative voiding in the case of urinary tract involvement.¹² A definitive diagnosis of endometriosis requires visual confirmation of the lesion during laparoscopy, and histologic confirmation of the presence of both ectopic endometrial glands and stroma.¹²

Interstitial cystitis, or pelvic pain of bladder origin, is another disorder that may be associated with CPP.⁸ The cause of IC is unclear, but it is thought to be multifactorial and progressive, involving bladder epithelial dysfunction, mast cell activation, and bladder sensory nerve upregulation (**Figure 1**).¹³⁻¹⁵ Estimates of the prevalence of IC in the United States range from 10 to 510/100 000 cases.^{16,17} Recent evidence suggests that this condition may, in fact, be much more prevalent than current estimates.^{14,18}

The symptoms of IC include urinary urgency/frequency and/or pelvic pain in the absence of urinary tract infec-

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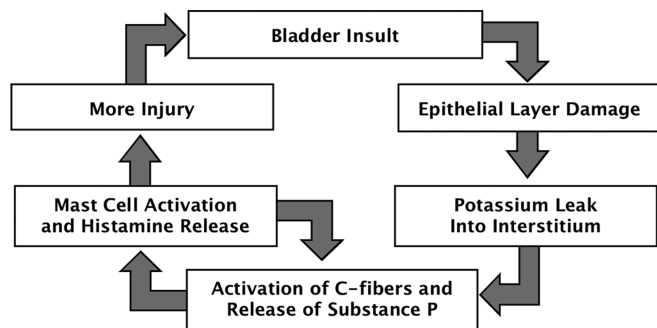


Figure 1. Proposed cycle of etiology of interstitial cystitis.¹⁴ Adapted from Evans RJ. Treatment approaches for interstitial cystitis: multimodality therapy. *Rev Urol.* 2002;4(suppl 1):S16–S20.

tion. Patients may also report dyspareunia and/or cyclic pain in association with the menses.^{14,19} Some patients may present with only urologic symptoms; conversely, 15% of patients present with chronic pain and no urologic symptoms.¹⁴ Patients with early IC may have only 1 or 2 symptoms, whereas at later stages, the full spectrum of symptoms may emerge and bladder capacity may be reduced.²⁰ Recent data suggest that outcomes may be improved when IC is detected and treated at earlier stages.

The Potassium Sensitivity Test (PST) was developed by Parsons et al^{14,15,21} to indicate abnormal permeability of the bladder epithelium, which is thought to play a central role in the pathophysiology of IC. Use of the PST has been validated in a number of studies,^{18,19,22,23} and may be used to help confirm the diagnosis of IC, particularly at earlier stages of the disease.

In a previously published retrospective review,⁹ we diagnosed biopsy-confirmed active endometriosis in 81% of patients with IC who had undergone concurrent laparoscopy and cystoscopy with hydrodistention in evaluation for CPP. Those findings suggested that these 2 conditions often exist concomitantly, and that the diagnosis of one condition should not preclude evaluation for the other. The objective of this study was to incorporate the use of the PST along with cystoscopy/hydrodistention and laparoscopy to prospectively determine the prevalence of IC and endometriosis in patients with CPP.

METHODS

This prospective evaluation included 178 women aged 18 to 60 years who presented from October 2000 to November 2002 at the Midwest Regional Center for Chronic Pelvic Pain and Bladder Control. Subjects were selected for this study based on the presence of abdominal/pelvic,

uterine, uterine sacral, and bladder/anterior vaginal wall tenderness during a physical examination. Symptoms of CPP had persisted for more than 6 months and included dyspareunia, dysmenorrhea, and low abdominal pelvic pain with or without irritative voiding symptoms, such as urinary frequency, urgency, nocturia, hesitancy, and sensation of incomplete emptying. Laboratory studies included a urinalysis, urine cytology, and urine and genital cultures. In addition, mycoplasma and urealyticum cultures were performed from the vaginal fornix. Negative culture results, including those for cytology, were required for enrollment.

All patients were tested for bladder potassium sensitivity using the PST as previously described by Parsons et al,^{21,22} and all patients underwent concurrent laparoscopic, cystoscopic, and bladder hydrodistention evaluations. A diagnosis of endometriosis was confirmed by biopsy and treated by surgical excision. The criteria used for a diagnosis of endometriosis included the pathologist-confirmed presence of ectopic glands and stroma.

Cystoscopy and hydrodistention were performed either before or after the laparoscopic evaluation. Bladder hydrodistention was conducted using sterile water with 80cm to 100cm of passive hydrostatic pressure being applied. The bladder was distended for a minimum of 2 minutes, and then the water was slowly drained. The submucosal petechial hemorrhages, or glomerulations, were observed as the bladder emptied, or during a second filling of the bladder. The diagnosis of IC was based on the National Institutes of Health–National Institute of Diabetes and Digestive and Kidney Diseases (NIH-NIDDK) guidelines, including the presence of 10 glomerulations per quadrant in 3 of the 4 quadrants of the bladder cavity and the presence of terminal hematuria.²⁴

RESULTS

Presenting Symptoms

All patients in this study presented with both bladder base and uterine tenderness on physical examination. Overall, 145 (81%) of the 178 study subjects with CPP had irritative urinary symptoms suggestive of overactive bladder.

Results of Cystoscopy with Hydrodistention and Laparoscopy

Diagnosis and PST results for patients in this study are shown in **Figure 2**. Of the 178 patients evaluated, 159 (89%) exhibited cystoscopic findings of IC, 134 (75%) had

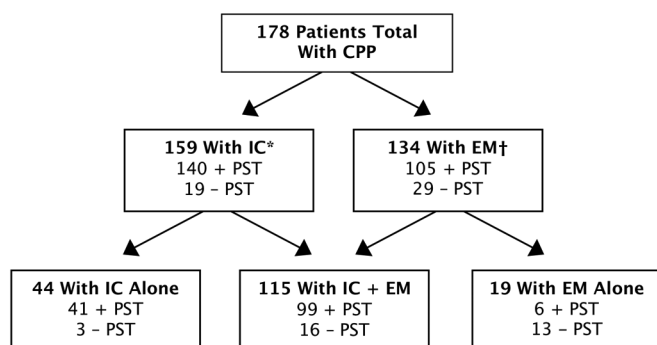


Figure 2. Diagnosis and PST results for patients in this study. CPP=chronic pelvic pain; EM=endometriosis; IC=interstitial cystitis; PST=Potassium Sensitivity Test. *Glomerulations and hematuria according to the National Institutes of Health–National Institute of Diabetes and Digestive and Kidney Diseases guidelines. †Presence of pathologist-confirmed presence of ectopic gland stroma.

a diagnosis of endometriosis based on histologic evaluation, and 115 (65%) were diagnosed with both conditions. In addition, 19 (11%) patients had endometriosis with no diagnosis of IC, and 44 (25%) had confirmed IC without endometriosis. The 159 patients with IC met the NIH-NIDDK guidelines for IC with the presence of glomerulations and hematuria. The diagnosis of IC was confirmed by experienced urologists who were involved in clinical research for treatment of IC.

Results of Potassium Sensitivity Testing–Relationship With Cystoscopic Results

Among the total study population of 178 patients, a positive PST was found in 146 (82%) patients. Of these 146 patients, 114 (78%) had irritative voiding symptoms. In addition, cystoscopic evidence of IC was found in 140 (96%) patients and, based on laparoscopic findings, endometriosis was demonstrated in 105 (72%).

In the original subgroup of 159 patients with cystoscopic evidence of IC, 140 (88%) showed increased potassium sensitivity based on the PST, and 129 (81%) had urologic symptoms of urinary urgency and frequency. Cystoscopic evidence of IC was found in 19 (12%) patients who had a negative PST, and 15 of those patients presented with irritative voiding symptoms.

DISCUSSION

In this study, we have shown that endometriosis and IC often exist concomitantly in patients with CPP who present with uterine and bladder tenderness. Among the

134 patients with endometriosis, 86% were also diagnosed with IC. Conversely, among the 159 patients with IC, 72% were also found to have endometriosis. We have therefore prospectively confirmed our earlier published results that IC and endometriosis have a high rate of overlap in this group of patients. As the patients in this study were selected for both uterine and bladder tenderness, the rate of overlap between gynecologic and urologic diagnoses is likely to be higher than in the general population of patients with CPP. However, these results emphasize the need for a careful physical examination and symptom history in patients with CPP, and the need to perform concurrent cystoscopy with hydrodistention and laparoscopy. If cystoscopy had been performed only in patients with irritative voiding symptoms/overactive bladder, a diagnosis of IC would have been missed in approximately 20% of patients.

Other studies have also found that IC is frequently diagnosed in patients with CPP, and that it overlaps to a high degree with other diagnoses. In one study²⁵ of 45 patients from general gynecologic practices who were scheduled to undergo laparoscopy for CPP, 17 (38%) were found to have IC based on the presence of irritative voiding symptoms and positive cystoscopic findings. In that study, 7 (41%) women diagnosed with IC also had endometriosis. Endometriosis was also diagnosed in 14 (50%) women who did not have IC. Notably, 30 (67%) of the women in that study had clinical symptoms of urgency and frequency or nocturia, and 10 women who were IC-negative had at least 10 glomerulations per quadrant noted in only 2 quadrants of the bladder. These results suggest that some women may have had early IC that did not meet the stringent NIDDK criteria for a diagnosis of IC.²⁵

A questionnaire-based study evaluated the prevalence of concomitant disease in individuals with diagnosed IC.²⁶ In this study in which patients with IC were not selected for CPP or gynecologic symptoms, the prevalence of endometriosis was approximately 17%. By comparison, the prevalence of endometriosis in the general population is estimated to be 1% to 7%.¹² In this survey, patients with IC were also found to be substantially more likely than the general population to have various autoimmune disorders, such as inflammatory bowel disease (100-fold greater risk) and systemic lupus erythematosus (30- to 50-fold greater risk), although these conditions were still relatively rare compared with other concomitant illnesses. The cause of both IC and endometriosis is thought to include an immune component, suggesting a possible pathophysiologic basis for the increased risk of one condition with the other.²⁶

In this study, we have shown that the PST is reasonably good at detecting the presence of IC: 96% (140) of patients with a positive PST had cystoscopic findings compatible with IC. Only 3.4% (6) of patients with a positive PST were cystoscopically negative. Previous studies have also reported that the rate of false positives is very low with the PST.^{22,23,27-29} These results indicate that a positive PST may be sufficient to indicate a diagnosis of IC.²² However, in our study, 12% (19) of women with cystoscopically confirmed IC had a negative PST, suggesting that, in the case of a negative PST, cystoscopy should still be performed.

Simple conservative methods are available for treating IC, including diet, pelvic floor physical therapy, and medications like hydroxyzine and pentosan polysulfate sodium (Elmiron[®], Ortho-McNeil Pharmaceutical, Inc, Raritan, NJ). Recent published articles have indicated the efficacy of oral contraceptives in treating IC and CPP.^{30,31} Many thought-leaders believe that the treatment of women with CPP has often been ineffective because the underlying cause is actually urologic rather than gynecologic.³² Therefore, it is reasonable to conclude that ineffective management of CPP and treatment failures may be the result of missed diagnoses of IC.

CONCLUSION

This study demonstrates that patients with CPP may have IC, endometriosis, or both conditions concomitantly. It is therefore imperative to evaluate the patient for both conditions, even when the diagnosis of one has been confirmed. When possible, cystoscopy with hydrodistention should be performed concurrently with laparoscopy to eliminate the need for a second procedure with the patient under general anesthesia and to facilitate the rapid detection and treatment of IC. A positive PST may be considered sufficient to diagnose IC and to begin treatment. A negative PST is not sufficient to rule out the presence of IC and should be followed up with cystoscopy. In the evaluation of the female with CPP, consideration should be given to the bladder as a source of pain early in the diagnostic workup.

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