

# Treatment of ulcerative compared to non-ulcerative interstitial cystitis with hyperbaric oxygen: a pilot study

David L. Wenzler, Farris Gulli, Maureen Cooney, Michael B. Chancellor, Jason Gilleran and Kenneth M. Peters

*Ther Adv Urol*

2017, Vol. 9(12) 263–270

DOI: 10.1177/  
1756287217731009

© The Author(s), 2017.  
Reprints and permissions:  
[http://www.sagepub.co.uk/  
journalsPermissions.nav](http://www.sagepub.co.uk/journalsPermissions.nav)

## Abstract

**Background:** The etiology of interstitial cystitis (IC) is often idiopathic but can be due to Hunner’s ulcers. Hyperbaric oxygen (HBO) is used to treat ulcerative disease of the superficial skin. We hypothesized that HBO can treat ulcerative IC (UIC) but would be less efficacious for non-ulcerative IC (NIC).

**Methods:** Patients with NIC and UIC enrolled in this study. Following informed consent, demographic information was collected. A visual analog pain scale and validated questionnaires were collected; each patient underwent cystoscopy prior to treatment. Each subject met with a hyperbaric specialist and after clearance underwent 30 treatments over 6 weeks. Adverse events were monitored. Patients repeated questionnaires, visual analog pain scale and global response assessment (GRA) immediately, 2 weeks, 3, 6 and 12 months after treatment. Patients also underwent cystoscopy 6 months after treatment. Differences before and after treatment were compared.

**Results:** Nine patients were recruited to this study. One was unable to participate, leaving two subjects with NIC and six with UIC. All patients completed HBO without adverse events. Three patients completed HBO but pursued other therapies 7, 8.5 and 11 months after treatment. On GRA, 83% of patients with UIC were improved. This treatment effect persisted, as 66% of UIC patients remained better at 6 months. In contrast, only one patient in the NIC group improved. Questionnaire scores improved in both groups. Pain scores improved by 2 points in the UIC group but worsened by 1.5 points in the NIC group. Two patients with ulcers resolved at 6-month cystoscopy.

**Conclusion:** HBO appeared beneficial for both UIC and NIC. Data shows slightly better benefit in patients with UIC compared to NIC; both groups showed improvement. Given the small sample size, it is difficult to draw definitive conclusions from these data. Larger studies with randomization would be beneficial to show treatment effect.

**Keywords** interstitial cystitis/painful bladder syndrome (IC/PBS), hyperbaric oxygen, treatment

Received: 2 April 2017; revised manuscript accepted: 20 August 2017.

## Introduction

Hyperbaric oxygen (HBO) therapy has been used in medicine for over a century. At atmospheric pressure and while breathing room air, approximately 0.3% of oxygen delivered to tissues is dissolved in plasma.<sup>1</sup> The remaining oxygen is delivered bound to hemoglobin. Henry’s Law states that the partial pressure of gas dissolved in liquid is equal to the partial pressure of the gas at the surface.<sup>2</sup> As a result,

breathing 100% oxygen as opposed to room air (21% oxygen) should increase the amount of oxygen in the blood. Boyle’s Law states that the volume of a gas is inversely proportional to the pressure.<sup>2</sup> This allows for more oxygen molecules in the same volume at higher pressures. Combining the modalities of 100% oxygen and increased atmospheric pressure allows for a 10–15-fold increase in the oxygen content in blood.

Correspondence to:  
**David L. Wenzler**  
Beaumont Health System,  
3601 W 13 Mile Rd., St.  
438, Royal Oak, MI 48073-  
6769, USA  
[dwenzler@urologist.org](mailto:dwenzler@urologist.org)

**Farris Gulli**  
**Maureen Cooney**  
**Michael B. Chancellor**  
**Jason Gilleran**  
**Kenneth M. Peters**  
Beaumont Health System,  
Royal Oak, MI, USA

Various indications for HBO include osteomyelitis, chronic wounds, burns and radiation cystitis.<sup>3-6</sup> While not completely understood, the physiology that assists with wound healing is believed to be due to increased oxygen in the blood and subsequent increase in oxygen delivery to tissues. Increased oxygen increases the amount of reactive oxygen species. These are parts of normal metabolism of many cell components and coordinate cell signaling and antioxidant pathways, which can improve wound healing.<sup>7</sup> HBO also induces production of VEG-F, which stimulates angiogenesis.<sup>8</sup>

One of the most promising applications of HBO is in the treatment of superficial skin ulcers. In the treatment of diabetic foot ulcers, HBO therapy increased the rate of ulcer healing and size of the ulcer during treatment.<sup>9</sup> In urology, ulcers in the bladder were first documented by Hunner in 1915.<sup>10</sup> These eventually became known as Hunner's ulcers and have been documented in cases of interstitial cystitis (IC). To date, several trials of HBO have been conducted for patients with IC. None of these trials directly compared the response to HBO in patients with the diagnosis of IC with and without Hunner's ulcers. We hypothesize that patients with ulcerative interstitial cystitis (UIC) will respond better to HBO than patients with non-ulcerative interstitial cystitis (NIC).

### Materials and methods

Patients with either a diagnosis of UIC or NIC were offered the option to participate in this IRB-approved study by their urologist (KP or JG). Potential participants met with a research nurse (MC) to determine whether they were eligible for the study. Inclusion criteria included a diagnosis of IC made by a urologist, history of previous treatments for IC and urinary frequency of at least eight times daily. Exclusion criteria were as follows: previous bladder or neurologic surgery (except for cystoscopic procedures), active urinary tract infection and chronic urinary retention requiring an indwelling catheter or intermittent catheterization. If patients met these criteria, informed consent was obtained. This was obtained by one of the authors (MC). All participants agreed not to undergo any treatments for IC during the course of the study.

All patients met with a hyperbaric medicine specialist (FG) for a history and physical examination

and a chest X-ray. The specialist determined whether or not the patient was able to undergo HBO treatment, in accordance with known contraindications for HBO.

If all of these criteria were met, demographic information (age, gender, past surgical history) was then collected. Participants then completed a voiding diary, validated questionnaires, IC Problem Index (ICPI) and IC Symptom Score Index (ICSI), visual analog scale (VAS) pain score and cystoscopy prior to beginning HBO treatment. Cystoscopy was completed by one of the urologists (KP, MBC, DW or JG).

HBO treatment included a total of 30 treatments. For each treatment, the patient is placed in a chamber set at 2.2 atm. They wear a hood and breathe 100% oxygen for 90 minutes. They spend 10 minutes in descent, receive two 10-minute breaks during the 90 minutes, and then spend 10 minutes in ascent. The total treatment time is 2 hours and 10 minutes. These were performed Monday through Friday for 6 weeks consecutively. If a patient missed a treatment, they underwent 'makeup' treatments until they received 30 treatments. Blood pressure, pulse and blood glucose were tested before and after each visit. Also at each visit, patients were monitored by a nurse and seen by a hyperbaric specialist and monitored for adverse events.

Patients had repeat visits with the research nurse at the following intervals after completing HBO: 2 weeks, 3 months, 6 months and 12 months. Each visit included an interval history, monitoring for any adverse events or side effects from HBO and completion of a voiding diary, ICPI and ICSI questionnaires, VAS pain score and global response assessment (GRA) to judge response to the treatment. The GRA scoring system is shown in Table 1. The following voiding diary variables were also noted before and after treatment: number of voids per day less than 30 cc, number of incontinence episodes per day and number of pads used per day. Cystoscopy was repeated 6 months after treatment to see if there were changes or if ulcers that were seen pre-treatment had resolved. In every case, post-treatment cystoscopy was done by the same urologist who performed the pre-treatment cystoscopy.

Data were then collected and analyzed by a statistician. Descriptive statistics were supplied. Our primary outcome is the GRA. Secondary outcomes

**Table 1.** Global response assessment (GRA).

	Markedly worse	Moderately worse	Mildly worse	Unchanged	Mildly better	Moderately better	Markedly better
GRA score	-3	-2	-1	0	+1	+2	+3

**Table 2.** Comparisons of demographic variables between ulcerative and non-ulcerative groups.

	Group A	Group B
Mean age (years)	54.2	47
Gender		
Male	2 (33.3%)	0
Female	4 (66.7%)	2 (100%)

included improvement in symptoms as seen in voiding diary, validated questionnaire scores, VAS pain score and cystoscopic appearance of the bladder.

## Results

A total of nine patients were recruited to participate in the study over a 2-year period. One patient was excluded due to frequent headaches. Of the eight patients that underwent HBO, six had UIC (Group A) and two had NIC (Group B). Differences in demographic information between the groups are shown in Table 2.

All eight patients completed hyperbaric treatment without adverse events. Three patients withdrew within the year at 7, 8.5 and 11 months after treatment. These patients were considered non-responders and excluded from any further analysis. Therefore, the total analyzed sample included four patients with UIC and one with NIC.

GRA was the primary outcome. All GRA responses are shown in Table 3. All five patients were improved on GRA after treatment. The NIC patient was markedly better as of 3 months after treatment, and this effect persisted at 12 months. In the UIC group, two patients were markedly better and two were mildly better.

Secondary outcomes included voiding diary responses, ICSI and ICPI questionnaire scores, VAS pain scores and resolution of ulcers on follow-up cystoscopy. Voiding diary responses were

extremely variable, both between groups, in each patient and before and after treatment. These responses were not used in any further analysis due to the lack of reproducibility.

ICSI scores for the analyzed patients are shown in Table 4. The one NIC patient analyzed showed a decrease from a pre-procedure score of 8 down to 1. Of the four UIC patients, median ICSI score decreased from 13 to 10.

ICPI scores are shown in Table 5. The NIC patient showed a decrease in ICPI score from 9 to 0. Median ICPI score in the UIC group decreased from 12 down to 10.

VAS pain scores were improved or stable in all patients. VAS pain scores are shown in Table 6. Median decrease in pain score was 1.5 points.

Three patients had ulcers prior to treatment. Two of these patients had resolution of their ulcers 6 months after treatment.

## Discussion

IC is notoriously difficult to diagnose and treat. Even the most recent AUA guidelines regarding the treatment of IC are very non-specific. They offer a variety of treatments for IC, which range from stress relief to physical therapy to oral medications to intravesical installations.<sup>11</sup> In addition, a large portion of these treatments are based upon expert opinion, which are the lowest level of evidence per the guidelines. IC patients are frustrated by attempting treatment options, often multiple, before they find an effective treatment that works for them. It is estimated by several studies that the cost of treatment of IC is estimated at \$230 million.<sup>12-17</sup>

One of the more severe types of IC is that in which patients have ulcers in the bladder. These were first documented by Hunner in 1915.<sup>10</sup> Since then, many authors have attempted different treatments for Hunner's ulcers, including transurethral fulguration, adrenocorticotropic hormone, heparin, hydrocortisone, prednisone and

**Table 3.** Global response assessment for all patients.

Patient	2 weeks	3 months	6 months	12 months
Ulcerative 1	+2	+2	+1	+1
Ulcerative 2	+1	-3	+1	+3
Ulcerative 3	+2	+1	+1	+3
Ulcerative 4	+2	+1	+1	+1
Non-ulcerative	+1	+3	+3	+3

**Table 4.** Interstitial Cystitis Symptom Score Index scores for all patients enrolled in the trial.

Patient	Pre-treatment	2 weeks	3 months	6 months	12 months
Ulcerative 1	14	7	8	10	9
Ulcerative 2	16	15	15	15	15
Ulcerative 3	11	6	10	8	2
Ulcerative 4	9	4	5	9	7
Non-ulcerative	8	6	4	1	1

**Table 5.** Interstitial Cystitis Problem Index scores for all patients enrolled in the trial.

Patient	Pre-treatment	2 weeks	3 months	6 months	12 months
Ulcerative 1	13	6	5	7	8
Ulcerative 2	13	13	13	12	12
Ulcerative 3	16	12	12	8	2
Ulcerative 4	10	6	7	5	8
Non-ulcerative	9	8	3	1	0

pentosanpolysulfate, all with varying degrees of success.<sup>18-23</sup> Some authors have even performed cystectomy in very severe cases.<sup>24</sup>

HBO has shown promise in several fields of medicine, including urology. A review in 2011 found that HBO has been used to treat Fournier's gangrene, radiation cystitis, IC, fistula and cyclophosphamide-induced cystitis.<sup>25</sup> It was first used to treat IC by van Ophoven and colleagues in 2004.<sup>26</sup> This pilot study examined six patients, of which four showed long-term improvement. The other two patients showed short-term improvement that was not sustainable. This pilot study led the same group to investigate further in 2006.<sup>27</sup> In this double-blind study, HBO treatment showed improvement in three of the patients who received it, with no improvement in the sham group. While promising, these data only showed improvement in three patients, and given the

intensity of HBO treatment this may be too much for patients to undergo with what appears to be a low benefit.

These initial investigations led to further clinical trials. In 2007, Tanaka and colleagues treated two women resistant to other therapies with 20 sessions of HBO.<sup>28</sup> One patient with a Hunner's ulcer showed complete resolution. One patient had Eustachian tube dysfunction resulting in persistent hearing dysfunction. Similar to the trials by van Ophoven and colleagues, this group then performed a longer-term, larger study.<sup>29</sup> This trial enrolled 11 patients, of whom seven showed improvement. One drawback, however, was a lack of standardization of the treatments, as patients either underwent treatment for 2 or 4 weeks. There was also no control group, which makes it difficult to directly attribute symptom improvement to HBO.

**Table 6.** Visual analog scale pain scores for all subjects.

Patient	Pre-treatment	2 weeks	3 months	6 months	12 months
Ulcerative 1	2	0	0	2	0
Ulcerative 2	3	4	0	1	1
Ulcerative 3	5	3	4	2	0
Ulcerative 4	3	1	3	2	3
Non-ulcerative	1	1	3	0	0

The summarized data above show much promise for HBO. As mentioned in the introduction, our theory was that patients with UIC would respond better than those with NIC given that HBO has been shown to improve ulcerative diseases elsewhere in the body. To this end, we made the goal of recruiting UIC and NIC patients and treating both to see if one had a greater response than the other. We were able to recruit both types of patients, and all underwent the same number of HBO treatments and completed the same questionnaires. We also excluded all the patients who pursued treatment before completion of the year assessment to minimize confounders that could have improved their symptom response.

Overall, patients responded well. There were no adverse events noted due to HBO. GRA showed improvement in both groups, and this effect was sustainable at 1 year post-treatment. All secondary outcomes, VAS pain, ICSI and ICPI scores were also improved in both groups. Given the small size of the groups, we were unable to directly compare the responses between them in a statistically significant way. One of the more promising findings in our study is that of the three patients with ulcers; two of them experienced cystoscopic resolution of the ulcers 6 months after treatment with HBO. Given the absence of other treatments during this time period (including fulguration), this suggests that HBO was the main reason for healing of these ulcers.

Given this is a clinical study, we are unable to explain how or why HBO is effective in IC. Yilmaz and colleagues attempted to explain pathologic and histologic changes in rats treated with HBO after hydrochloric acid-induced IC.<sup>30</sup> Rats with induced IC and treated with HBO showed reduced mast cell activity. Other markers of cell damage also were improved if treated with HBO. This is a basic science study that begins to shed light on how HBO can ameliorate some of the

symptoms of UIC, which are largely due to inflammation.

Our study has many advantages. This is the first study performed to our knowledge that directly compares treatment response in patients with UIC and NIC. In addition, all of the patients in our study were treated with the same type and number of HBO sessions. This is advantageous because other studies used varying numbers of treatments not only within treatment groups but also between groups. The use of validated questionnaires to assess treatment effect is also a benefit. This provides consistency and validity to our results. Lastly, we excluded women who had previous urinary tract surgeries, such as bladder suspension, pelvic organ prolapse repair and surgeries for stress incontinence. It is documented in several studies that any of these surgeries can affect pelvic pain, discomfort, quality of life and sexual function.<sup>31–36</sup>

While promising, our study does have its disadvantages. First, the study had a very small number of subjects. As a result, we were unable to directly compare groups and draw any statistical significance from our data. Second, while we excluded patients that underwent surgical or medical treatments, we did not assess what non-medical treatments, such as diet, exercise, stress relief or physical therapy patients were simultaneously undergoing during and in the year following treatment. Several authors have advocated for the use of these techniques and how they can help with IC symptoms.<sup>11,37–39</sup> It would be difficult to assess specific non-medical therapies that patients underwent during treatment and even more challenging to control for these. Third, it is well-documented that other syndromes commonly occur with IC. These can include, but are not limited to, inflammatory bowel disorders, endometriosis, chronic pelvic pain, vulvodynia, overactive bladder, fibromyalgia, chronic pain and chronic fatigue

syndrome.<sup>40–45</sup> In a study where it is difficult to recruit patients (more on that below), it would be very challenging to exclude subjects who have any of these concomitant medical conditions. If subjects do have these conditions, it is impossible to know if HBO has any effect on these other medical problems and if the treatment of these could improve symptoms.

From a study standpoint, recruitment proved challenging – the time commitment is intense and the lack of pursuing other treatments for a year after the study were the primary deterrents. This is largely the reason many of our patients were either unemployed, on disability or worked part-time. The study was also expensive and performing the study for only eight patients still cost a significant amount. Repeating the study with more patients would be beneficial to prove statistical significance. This would likely require corporate sponsorship or a generous grant to complete, given the aforementioned financial difficulties.

### Conclusion

Our study is the first to our knowledge that directly compares HBO treatment response in UIC and NIC. Despite the limitations, our study is helpful in identifying a potential response difference between the two groups. Further validation with a larger sample size would be useful.

### Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

### Conflict of interest statement

The authors declare that there is no conflict of interest.


### References

- Pittman RN. Regulation of Tissue Oxygenation. In: *Integrated systems physiology: from molecule to function to disease*. San Rafael, CA: Morgan & Claypool Life Sciences, 2011.
- A Dictionary of Physics*. San Rafael, CA: Morgan & Claypool Life Sciences, 2011.
- Mader JT, Adams KR, Wallace WR, *et al*. Hyperbaric oxygen as adjunctive therapy for osteomyelitis. *Infect Dis Clin North Am* 1990; 4: 433–440.
- LaVan FB and Hunt TK. Oxygen and wound healing. *Clin Plast Surg* 1990; 17: 463–472.
- Wiseman DH and Grossman AR. Hyperbaric oxygen in the treatment of wounds. *Crit Care Clin* 1985; 1: 129–145.
- Kindwall EP. Hyperbaric oxygen treatment of radiation cystitis. *Clin Plast Surg* 1993; 20: 589–592.
- Thom SR. Hyperbaric oxygen: its mechanisms and efficacy. *Plast Reconstr Surg* 2011; 127: 131–141.
- Lee C, Chen S, Tsai S, *et al*. Hyperbaric oxygen induces VEGF expression through ERK, JNK, and c-Jun/AP-1 activation in human umbilical vein endothelial cells. *J Biomed Sci* 2006; 13: 143–156.
- Kranke P, Bennett MH, Martyn-St James M, *et al*. Hyperbaric oxygen therapy for chronic wounds. *Cochrane Database Syst Rev* 2015; 24: 6.
- Hunner GL. A rare type of bladder ulcer in women: report of 8 cases. *Boston Med Surg J* 1915; 172: 660–664.
- Hanno PM, Burks DA, Clemens JQ, *et al*. AUA Guideline for the diagnosis and treatment of interstitial cystitis/bladder pain syndrome. *J Urol* 2011; 185: 2162–2170.
- Anger JT, Zabihi N, Clemens JQ, *et al*. Treatment choice, duration, and cost in patients with interstitial cystitis and painful bladder syndrome. *Int Urogynecol J* 2011; 22: 395–400.
- Wu EQ, Birnbaum H, Mareva M, *et al*. Interstitial cystitis: cost, treatment and co-morbidities in an employed population. *Pharmacoeconomics* 2006; 24: 55–65.
- Stanford EJ, Chen A, Wan GJ, *et al*. Treatment modalities, health care resource utilization, and costs in patients diagnosed with interstitial cystitis. *Am J Obstet Gynecol* 2008; 199: e1–e10.
- Wu EQ, Birnbaum H, Kang YJ, *et al*. A retrospective claims database analysis to assess patterns of interstitial cystitis diagnosis. *Curr Med Res Opin* 2006; 22: 495–500.
- Riedl C, Engelhardt P and Schwarz B. Treatment costs of bladder pain syndrome/interstitial cystitis in Austria: a pharmacoeconomic approach

- following current guidelines. *Clin Drug Investig* 2013; 3: 737–742.
17. Clemens JQ, Meenan RT, Rosetti MC, *et al.* Costs of interstitial cystitis in a managed care population. *Urology* 2008; 71: 776–780.
  18. Kreutzmann HA. Treatment of Hunner's ulcer of the bladder by fulguration. *Cal State J Med* 1922; 20: 128–130.
  19. Burke J and Vernon HK. Effect of ACTH on Hunner's ulcer of the urinary bladder. *Br Med J* 1952; 2: 477.
  20. Karpati F. Treatment of ulcer simplex of the urinary bladder (Hunner's ulcer) with heparin. *Orv Hetil* 1965; 106: 1277–1278.
  21. Johnston JH. Local hydrocortisone for Hunner's ulcer of the bladder; preliminary report. *Br Med J* 1956; 2: 698–699.
  22. Jepsen JV, Sall M, Rhodes PR, *et al.* Long-term experience with pentosanpolysulfate in interstitial cystitis. *Urology* 1998; 51: 381–387.
  23. Soucy F and Gregoire M. Efficacy of prednisone for severe refractory ulcerative interstitial cystitis. *J Urol* 2005; 173: 841–843.
  24. Peters KM, Jaeger C, Killinger KA, *et al.* Cystectomy for ulcerative interstitial cystitis: sequelae and patient perceptions of improvement. *Urology* 2013; 82: 829–833.
  25. Gallego Vilar D, Garcia Fadrique G, Povo Martín IJ, *et al.* Hyperbaric oxygen treatment in urology. *Arch Esp Urol* 2011; 64: 507–516.
  26. Van Ophoven A, Rossbach G, Oberpenning F, *et al.* Hyperbaric oxygen for the treatment of interstitial cystitis: long-term results of a prospective pilot study. *Eur Urol* 2004; 46: 108–113.
  27. Van Ophoven A, Rossbach G, Pajonk F, *et al.* Safety and efficacy of hyperbaric oxygen therapy for the treatment of interstitial cystitis: a randomized, sham controlled, double-blind trial. *J Urol* 2006; 176: 1442–1446.
  28. Tanaka T, Kawashima H, Makino T, *et al.* Hyperbaric oxygen therapy for interstitial cystitis resistant to conventional treatments. *Int J Urol* 2007; 14: 563–565.
  29. Tanaka T, Nitta Y, Morimoto K, *et al.* Hyperbaric oxygen therapy for painful bladder syndrome/interstitial cystitis resistant to conventional treatments: long-term results of a case series in Japan. *BMC Urol* 2011; 11: 11.
  30. Yilmaz M, Cakmak T, Yenilmez A, *et al.* Effects of hyperbaric oxygen therapy on hydrochloric acid-induced interstitial cystitis in rats: a histological and ultrastructural study. *Undersea Hyperb Med* 2016; 43: 181–188.
  31. Laganà AS, La Rosa VL, Rapisarda AM, *et al.* Comment on: Effect on sexual function of patients and patients' spouses after midurethral sling procedure for stress urinary incontinence: a prospective single center study. *Low Urin Tract Symptoms* 2017; 9: 62.
  32. Vitale SG, Caruso S, Rapisarda AM, *et al.* Biocompatible porcine dermis graft to treat severe cystocele: impact on quality of life and sexuality. *Arch Gynecol Obstet* 2016: 125–131.
  33. Caruso S, Bandiera S, Cavallaro A, *et al.* Quality of life and sexual changes after double transobturator tension-free approach to treat severe cystocele. *Eur J Obstet Gynecol Reprod Biol* 2010: 106–109.
  34. Laganà AS, La Rosa VL, Rapisarda AMC, *et al.* Pelvic organ prolapse: the impact on quality of life and psychological well-being. *J Psychosom Obstet Gynaecol* 2017: 1–3. DOI: <http://dx.doi.org/10.1080/0167482X.2017.1294155>
  35. Vitale SG, La Rosa VL, Rapisarda AMC, *et al.* The importance of a multidisciplinary approach or women with pelvic organ prolapse and cystocele. *Oman Med J* 2017; 32: 263–264.
  36. Friedlander JI, Shorter B and Moldwin RM. Diet and its role in interstitial cystitis/bladder pain syndrome (IC/BPS) and comorbid conditions. *BJU Int* 2012; 109: 1584–1591.
  37. Karper WB. Exercise effects on interstitial cystitis: two case reports. *Urol Nurs* 2004: 202–204.
  38. O'Hare PG III, Hoffmann AR, Allen P, *et al.* Interstitial cystitis patients' use and rating of complementary and alternative medicine therapies. *Int Urogynecol J* 2013; 24: 977–982.
  39. Peters KM, Killinger KA, Mounayer MH, *et al.* Are ulcerative and nonulcerative interstitial cystitis/painful bladder syndrome two distinct diseases? A study of coexisting conditions. *Urology* 2011; 78: 301–308.
  40. Gardella B, Porru D, Ferdeghini F, *et al.* Insight into urogynecologic features of women with interstitial cystitis/painful bladder syndrome. *Eur Urol* 2008; 54: 1145–1151.

41. Cheng C, Rosamilia A and Healey M. Diagnosis of interstitial cystitis/bladder pain syndrome in women with chronic pelvic pain: a prospective observational study. *Int Urogynecol J* 2012; 23: 1361–1366.
42. Bogart LM, Berry SH and Clemens JQ. Symptoms of interstitial cystitis, painful bladder syndrome and similar diseases in women: a systematic review. *J Urol* 2007; 177: 450–456.
43. Peters KM, Carrico DJ and Diokno AC. Characterization of a clinical cohort of 87 women with interstitial cystitis/painful bladder syndrome. *Urology* 2008; 71: 634–640.
44. Chelimsky G, Heller E, Buffington CA, *et al.* Co-morbidities of interstitial cystitis. *Front Neurosci* 2012; 6: 114.
45. Laganà AS, Vitale SG, Trovato MA, *et al.* Full-thickness excision versus shaving by laparoscopy for intestinal deep infiltrating endometriosis: rationale and potential treatment options. *Biomed Res Int* 2016: 170–179. DOI: 10.1155/2016/3617179.

Visit SAGE journals online  
[journals.sagepub.com/  
home/tau](http://journals.sagepub.com/home/tau)

 SAGE journals