PILOT STUDY

Effect of BPC-157 on Symptoms in Patients with Interstitial Cystitis: A Pilot Study

Edwin Lee, MD; Christopher Walker, MD; Bahram Ayadi, BS

ABSTRACT

Context • Moderate to severe interstitial cystitis (also known as bladder pain syndrome) is a disabling disease with no effective treatment. Although pentosan polysulfate is an approved treatment for interstitial cystitis, some patients on this medication experience treatment failure after one year, and its long-term use has been linked to pigmentary maculopathy. The peptide Body Protective Compound 157 (BPC-157) is a possible treatment for interstitial cystitis but is currently not approved by the US Food and Drug Administration.

Objective • To assess the safety and efficacy of BPC-157 manufactured by a 503A compounding pharmacy as a treatment for interstitial cystitis.

Participants • Twelve women between the ages of 39 and 76 years with a mean age of 58.3 years participated in this trial at a private clinic. Of these, 10 were White, one was Asian, and one was Latina. None of the 12 women had responded to pentosan polysulfate.

Methods • The women underwent cystoscopy and were treated with injections of the peptide BPC-157 (total of 10 mg) around the area of inflammation of the bladder during a single procedure. Global Response Assessment questionnaire was given to all the subjects to assess the efficacy of BPC-157.

Results • Complete resolution of symptoms after one treatment was reported in 10 of 12 patients, who rated their success at 100%. The remaining 2 of 12 patients rated their success at 80%, with most symptoms resolved but about 20% of their symptoms lingering. No one dropped out of the study, and no adverse events were reported. This therapy was successful because all 12 patients scored a 5/5 on the Global Response Assessment.

Conclusion • This is the first report of intravesical BPC-157 (10 mg) injection to help patients with moderate to severe interstitial cystitis who did not respond to pentosan polysulfate treatment. (*Altern Ther Health Med.* 2024;30(10):12-17).

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INTRODUCTION

Interstitial cystitis

Moderate to severe interstitial cystitis is a disabling chronic bladder disorder also known as bladder pain syndrome. It presents with lower urinary tract symptoms, such as dysuria, dyspareunia, increased urinary frequency (often up to 60 times a day) and urinary urgency without urinary tract infection lasting for at least 6 weeks, causing pelvic pain and pressure or discomfort related to bladder filling. Interstitial cystitis can also present as pain outside the genital location, such as in the lower abdomen and back.[1,2] Interstitial cystitis is classified into 2 broad types: ulcerative and nonulcerative. Based on cystoscopic findings, interstitial cystitis can be classified based on severity from mild to severe.[3]

The discomfort that builds up due to bladder irritation can cause stress, fixation on the condition, and worry about recurrence, leading to anxiety and impairing the quality of life for people living with moderate to severe interstitial cystitis. Women are more likely than men to be diagnosed with interstitial cystitis. Interstitial cystitis can also occur in domestic cats (*Felis catus*) and has been reported sporadically in other mammals, including cheetahs, dogs, llamas, and potbellied pigs.[4,5]

The central role of inflammation has been confirmed in the pathogenesis of interstitial cystitis, although the etiology of interstitial cystitis remains mostly unknown.[6] Glycosaminoglycans make up a portion of the bladder mucosa. The absence of this protective layer of glycosaminoglycans in patients with interstitial cystitis

increases inflammation, which leads to cyst formation and swelling with subsequent pain and irritation.[7] In one study, approximately half of the women diagnosed with interstitial cystitis reported symptoms of dysuria.[8] Other causative factors of interstitial cystitis have been suggested, including chronic or subclinical infection, autoimmunity, and genetic susceptibility, any of which could be responsible for initiating the inflammatory response. Environmental, urinary microbiome and dietary factors can also influence the symptoms of interstitial cystitis.

Currently, no treatments capable of curing interstitial cystitis are available; however, some treatments exist that reduce the discomfort associated with the condition. These treatments can be delivered by bladder instillation or as oral medication. Pentosan polysulfate was endorsed by the US Food and Drug Administration (FDA) in 1996 and remains the only treatment approved for interstitial cystitis. Pentosan polysulfate can reduce inflammation of the bladder wall and restore the protective mucosal barrier. Pentosan polysulfate has been associated with pigmentary maculopathy, which diminishes visual capacity.[9] There has not been enough research to fully support the link between an abnormal immune response in patients with interstitial cystitis and the side effects linked to use of pentosan polysulfate.[10]

Dimethyl sulfoxide reduces pain and inflammation associated with interstitial cystitis. Dimethyl sulfoxide combined with intravesical cocktail therapy can lead to better outcomes after treatment, more effective reduction of inflammation, and higher quality of life for patients with interstitial cystitis.[7] Other therapies for interstitial cystitis include injecting or infusing hyaluronic acid, botulinum toxin A, triamcinolone, resiniferatoxin, and platelet-rich plasma. Several surgical options are available: ablation of the ulcerative lesions in the bladder, resection of ilioinguinal and iliohypogastric nerves, reconstructive surgery, and cystectomy.[11] In a review of 450 patients with severe interstitial cystitis who had undergone an operation, surgery was associated with a complication rate of 26.5% with an overall mortality of 1.3%.[12]

History of BPC-157

In 1993, Predrag Sikirić, MD, PhD, of Croatia isolated the peptide Body Protective Compound 157 (BPC-157) from human gastric juice.[13] In animal studies, BPC-157 has been shown to have many restorative properties.[14] It can help with repairing tendons, ligaments, muscles, nerves, bone fractures, teeth, and corneas and promote recovery from traumatic brain injury.[15-25] BPC-157 has been shown to reduce inflammation in different animal models.[26,27]

The pharmacokinetics, excretion, metabolism, and distribution profiles of BPC-157 were performed in rats and in beagle dogs. After intramuscular and intravenous administration of Tritium-labeled BPC-157, the elimination half-life of BPC-157 was less than 30 minutes. Among all doses used in rats and beagle dogs, BPC-157 showed linear pharmacokinetics. The main excretion pathways of BPC-157 involved the kidneys and biliary tract. BPC-157 is a 15 amino acid peptide, and in the metabolism study Tritium-labeled BPC-157 eventually metabolized into single amino acids that can be reused by the body.[28]

BPC-157 has been very popular among athletes and weightlifters, who have nicknamed it the Wolverine peptide. It has been used to help with the recovery of joint issues or partial muscle or tendon tears. Many people obtain it from online peptide websites, which sell it for research purposes only. Products sold by online peptide stores are concerning because they are unregulated for the safety of these substances. We strongly recommend obtaining injectable peptides from a 503A compounding pharmacy since they operate under the oversight of their state boards of pharmacy and adhere to the United States Pharmacopeia standards. In addition, these peptides are independently tested for endotoxins and stability. They are verified to contain the product on the label.[29]

Currently, only one study in humans using BPC-157 from a compounding pharmacy has been published. E.L. studied the use of intra-articular injection of BPC-157 for multiple types of knee pain. In that trial, 14 of 16 patients reported relief of their knee pain after one intra-articular injection of BPC-157. There were no reported side effects, and the treatment was well tolerated.[30] Moreover, BPC-157 is very safe. No adverse effects in clinical trials in animals were reported, nor was a lethal dose (LD1) achieved in toxicology studies.[14,31,32] An ongoing, institutional review board-approved, single-blinded prospective study by E.L. and colleagues is examining the efficacy of BPC-157 on the recovery rates in humans undergoing knee and shoulder surgery. In this study, we aimed to show the safety and efficacy of BPC-157 in 12 women with interstitial cystitis who have failed therapy with pentosan polysulfate.

METHODS

Study design/ Chart Review and Data Analysis

In January 2023 at the UroGyn Specialists of Florida clinic, an experimental trial had been conducted using the non–FDA-approved BPC-157 peptide to help treat patients with moderate to severe interstitial cystitis. All the participants had been informed that BPC-157 is an experimental peptide that has not been FDA approved in the United States. They had been told that only one human study of BPC-157 has been published, in which BPC-157 had been well tolerated and no side effects had been noted. They had been informed that BPC-157 was well tolerated during animal studies in which no serious adverse events were noted.

We conducted a retrospective study of these patients by doing a chart review from January 2023 to June 2024 at the UroGyn Specialists of Florida clinic in Orlando, Florida. All the patients had a baseline cystoscope, therapy with BPC-157, and a 6-week follow up with another cystoscope. They were contacted and were given the Global Response Assessment questionnaire to evaluate the patients' perceptions of treatment effectiveness. See Table 1 for the Global Response Assessment Scale. Most of the patients were contacted 4-6 months after

using BPC-157. Their ethnicity was collected, and all the data was kept confidential. Our data analysis rated patients' responses to treatment from being significantly worse to no change to being significantly better after therapy. Patients' responses were also evaluated to determine whether their age and ethnicity were related to any significant differences in their results.

Inclusion criteria

This study included patients with moderate to severe interstitial cystitis who had participated in the experimental trial conducted in January 2023 at the UroGyn Specialists of Florida clinic using the non–FDA-approved BPC-157 peptide. Men could have been included, but no men with moderate to severe interstitial cystitis were seen at the clinic.

Exclusion criteria

Patients who had signs of infection or a tumor in the bladder were excluded from the study as well as pregnant women and individuals 18 years old or younger.

Patients

The study included 12 women, predominantly White (10 patients), with 1 Asian participant and 1 Latina participant. The age range of the participants was 39 to 76 years, with a mean age of 58.3 years.

All of the participants had tried pentosan polysulfate, several for more than 5 years. None of them had used pentosan polysulfate for more than 6 months before the BPC-157 intravesical injections. None of the patients had signs of urinary infection, nor were any treated with any oral drugs or intravesical instillations 6 months prior to intravesical injection of BPC-157. All the patients paid for the BPC-157 and were given no honorarium to try this experimental therapy.

All 12 patients underwent a pelvic examination, urine analysis, and cystoscopy using a 30° cystoscope. The cystoscopy showed hypervascularity and hyperemia in their bladders, and some patients also had ulcers. All 12 patients had a diagnosis of moderate to severe interstitial cystitis.

Procedure

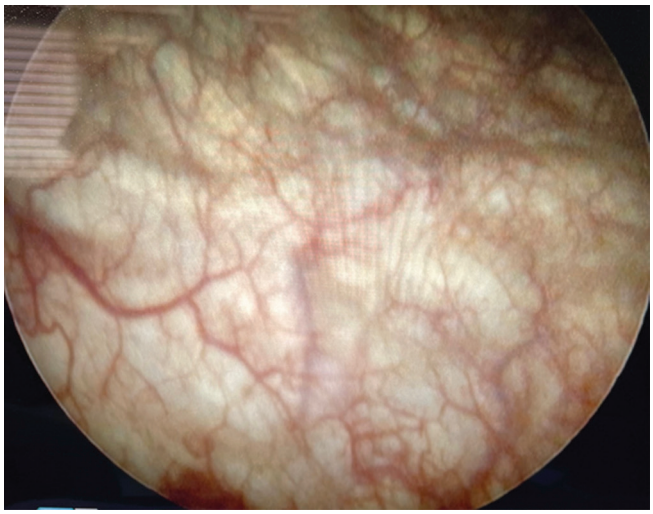
The peptide BPC-157 was obtained from a 503A compounding pharmacy in the United States that does not wish to disclose its name. The concentration of BPC-157 was 2 mg/mL; one vial contained 5 mL BPC-157 with a total dose of 10 mg. From January 2023 to June 2024, all patients underwent a transurethral endoscopic procedure during which they were given intravesical injections of 1 mg BPC-157, placed in 10 spots (total of 10 mg) in the uroepithelium of the bladder wall.

BPC-157 was administered through a 17-24F catheter 30° cystoscope with an injeTAK 70 cm needle. The injections of BPC-157 were in the regions of the dome and trigone of the bladder. The injections were equally distributed, using the injeTAK adjustable tip cystoscope needle and delivering the BPC-157 at a depth of 3 mm into the uroepithelium of the bladder wall.

Table 1. Global Response Assessment Scale

Number	Response	Grading (%)	Outcome
1	Significantly worse	0	Failure of the therapy
2	Somewhat worse	1 to 25	Failure of the therapy
3	Unchanged (neither worse nor better)	26 to 50	Failure of the therapy
4	Somewhat improved	51 to 75	Successful therapy
5	Significantly improved	76 to 100	Successful therapy

Figure 1. Before therapy of BPC-157. Urinary bladder with extensive vasculature, hyperemia with hypertrophy of the detrusor muscle



RESULTS

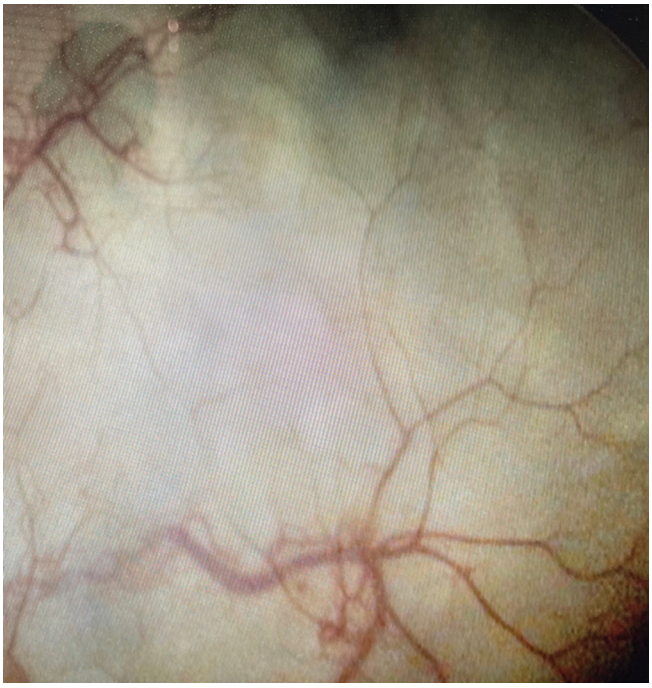
Retrospective chart review

The study had 12 participants who were followed up 6 weeks after BPC-157 administration. Of the 12 participants, 10 experienced complete resolution of their symptoms, a 100% improvement based on the Global Response Assessment questionnaire. Also, two of 12 participants had an 80% improvement of symptoms, with most of their symptoms resolved. Because all 12 patients scored a 5 on the Global Response Assessment, this therapy was considered successful. There was no relationship between the age or ethnicity of the patients who rated their improvement of symptoms at 80%.

Patients reported an improvement in their symptoms as early as 2 weeks after the procedure. The symptoms that improved first were urgency and frequency of urination. None of the participants experienced symptoms of fever, skin rash, nausea or vomiting, irritative urinary symptoms (urgency or frequency), or dyspareunia. No postprocedural complications of hematuria or acute cystitis were reported.

Figure 1 shows a cystoscopic image of one woman's bladder taken before therapy was initiated. She had been diagnosed with severe interstitial cystitis with hyperemia, hypervascularity, and hypertrophy of the detrusor muscles. Figure 2 shows a cystoscopic image of the same area of the same bladder 6 weeks after intravesical administration of 10 mg BPC-157. One can see resolution of the hypervascularity, hyperemia, and hypertrophy of the detrusor muscle.

Figure 2. 6 weeks post intravesical 10 mg of BPC-157 with the resolution of hyperemia, hypervasculature, and hypertrophy of the detrusor muscle



DISCUSSION

BPC-157 is a naturally derived peptide from human stomach fluid. Dr. Sikiric's team has investigated BPC-157's cytoprotective effects many times in different organs and tissues. Their studies reveal that BPC-157 provides potent cytoprotection against neural injury and gastrointestinal ulcers.[13,14] In a study on rats with persistent gastric ulcers given a high dose of 6-alpha-methylprednisolone, BPC-157 improved gastric ulcer mucosal healing and overcame the inhibitory effects of corticosteroids on the healing process.[33]

BPC-157 has also demonstrated cytoprotective properties in the gastrointestinal tract. Wang and colleagues investigated whether BPC-157 can attenuate 5-hydroxytryptamine, also known as serotonin.[34] The gut produces about 95% of the serotonin in the human body. The serotonin in the intestinal mucosa stimulates the production of proinflammatory mediators by immune cells. Enteric serotonin may be a key player in physiological actions and the pathogenesis of intestinal inflammation.[35,36] BPC-157 suppresses the synthesis and release of enteric serotonin and attenuates gastrointestinal motility in human and rat enteric samples.[21]

One study looked at the role of serotonin in a feline model of interstitial cystitis. Full-thickness bladder strips were isolated from aged-matched healthy control cats and cats with clinically verified feline interstitial cystitis. A serotonin dose response (0.01-10 μM) was determined for each strip with the mucosa intact or denuded. The authors concluded that feline interstitial cystitis increases detrusor contractile response to serotonin.[34] BPC-157 has been shown to suppress the release of enteric serotonin. This action is one of BPC-157's mechanisms in the therapy of interstitial cystitis. Compared to Figure 1, Figure 2 above shows the resolution of the hypervascularity, hyperemia and also the hypertrophy of the detrusor muscles. In the middle of Figure 1, the hypertrophic detrusor muscles appear as "small boxes/ridges." The therapy of intravesical injection of BPC-157 in this study successfully treated moderate to severe interstitial cystitis with resolution of hypervascularity, hyperemia and hypertrophic detrusor muscles.

BPC-157 was chosen for this study primarily because of its anti-inflammatory properties and its role in maintaining epithelial integrity. BPC-157 has been studied for the treatment of colitis and of ischemia and reperfusion in rats. BPC-157 reduces inflammation, restores the damaged endothelium, quickly replenishes blood supply to the ischemically injured area, and rapidly activates collateral circulation. BPC-157 has been shown to lower markers of oxidative stress.[37] The exact etiology of interstitial cystitis is unknown, but it can develop into a state of chronic inflammation.

BPC-157 has been studied extensively for healing wounds in animals. It has healed cutaneous wounds in the colon, stomach, esophagus, and small intestine.[37,38] It has also healed deep tissue wounds and fistulas in rodents.[39,40] Chemical burns can be particularly challenging to treat due to the nature of the injuries they cause, and there are no optimal therapies for them. Topical treatment with BPC-157 was shown to accelerate wound closure following an alkali burn in rats. Histological examination of burned skin sections with hematoxylin-eosin and Masson staining showed better granulation tissue formation, re-epithelialization, dermal remodeling, and a higher extent of collagen deposition than the untreated rats (control group). BPC-157 can promote healing through many pathways including the vascular endothelial growth factor (VEGF) expression in wounded skin tissues, extracellular signal–regulated kinases 1 and 2 (ERK1/2) as well as their downstream targets, including c-Fos, c-Jun, and early growth response protein 1.[16]

The carboxylic groups of BPC-157 may contribute to its role as an antioxidant. BPC-157 contains four carboxylic groups that may be involved as an antioxidant. Glutathione may play a role in the antioxidant properties of BPC-157.[41] Additionally, BPC-157 is present in most tissues, where it can bind reactive free radicals and inactivate them at crucial positions not reachable by other antioxidants.[44]

BPC-157 is involved with maintaining endothelial integrity.[13,14,33] BPC-157 also acts as a free radical scavenger, counteracts free radical–induced lesions, and normalizes nitric oxide levels in tissues and during ischemia and reperfusion.[31,42] BPC-157's many pleiotropic benefits involve the VEGFR2 and growth hormone receptors as well as distinctive pathways, including VEGFR2-AKT-eNOS, ERK1/2, FAK-paxillin, FoxO3a, p-AKT, p-mTOR and p-GSK-3β.[16,43-45]

VEGFR2-AKT-eNOS (vascular endothelial growth factor receptor 2 and AKT–endothelial nitric oxide synthase): Crucial for endothelial function and nitric oxide production, which support blood vessel health and repair.

ERK1/2 (extracellular signal–regulated kinases 1 and 2): Important for cell division, survival, and differentiation.

FAK-paxillin (focal adhesion kinase–paxillin): Involved in cell adhesion, migration, and signaling.

FoxO3a (forkhead box O3): Regulates cell cycle, apoptosis, and oxidative stress responses.

p-AKT (phosphorylated AKT): Plays a role in cell survival, growth, and metabolism.

p-mTOR (phosphorylated mechanistic target of rapamycin): Central regulator of cell growth, proliferation, and survival.

p-GSK-3β (phosphorylated glycogen synthase kinase 3 beta): Involved in glycogen metabolism, cell proliferation, and survival.

BPC-157 also interacts with the prostaglandin, dopamine, and serotonin systems, which are crucial for inflammation, pain modulation, mood regulation, and other physiological processes.[21,46,47] These combined interactions and pathways contribute to its potential therapeutic effects, including the treatment of interstitial cystitis by promoting tissue repair, reducing inflammation, and modulating pain pathways.

Intravesical BPC-157 (10 mg) injection has shown remarkable effectiveness for patients with moderate to severe interstitial cystitis for whom treatment with pentosan polysulfate failed. The 2 of 12 patients who had 80% improvement after one intravesical treatment of 10 mg BPC-157 are requesting another injection, for which they have been scheduled.

As of September 2023, the FDA has banned 503A compound pharmacies from producing many peptides due to the lack of data showing their safety and efficacy. The FDA has not restricted physicians from prescribing peptides. BPC-157 is on the list of banned peptides.[29] The FDA should seriously consider changing BPC-157 to category 1 (allowing 503A compounding pharmacy to produce peptides) from category 2 (not enough safety data) because of the extensive research in animals and lack of any toxic effects. Overall, BPC-157 is a very safe peptide, and lethal dose (LD1) was not achieved in toxicology studies.[14,31,32]

This study showed an excellent response to BPC-157 in 10 of 12 patients, while 2 of 12 patients had an 80% success rate. According to the Global Response Assessment, there was a 100% success rate with using intravesical BPC-157 (10 mg). No side effects were reported, and the treatment was well tolerated.

Limitations

Our study lacked a large sample size, ethnic variation, and sham control group. In addition, preoperative and postoperative biopsies would have been optimal but were not performed due to the extra cost.

CONCLUSION

Intravesical BPC-157 (10 mg) injection has shown remarkable effectiveness for patients with moderate to severe interstitial cystitis who have not responded to pentosan polysulfate. Complete resolution of symptoms after one treatment was reported in 10 of 12 patients. This therapy was successful because all 12 patients scored a 5/5 on the Global Response Assessment. No side effects were noted, and the treatment was well tolerated. BPC-157 is a natural peptide derived from human gastric fluid that offers multiple pleiotropic benefits by interacting with various receptors and signaling pathways. As such, it is a viable and inexpensive treatment option before considering surgery for patients with interstitial cystitis. Given the effectiveness and safety profile of BPC-157, the FDA should seriously consider reclassifying BPC-157 from category 2 (not enough safety data) to category 1 (allowing compounding pharmacies to produce peptides). This change would permit physicians to order this natural peptide for patients in need from FDA-regulated compounding pharmacies.

CONFLICT OF INTEREST

The authors declare there is no conflict of interest in the authorship or publication of this manuscript.

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