Surgical Therapies for Chronic Interstitial Cystitis

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INTRODUCTION

Interstitial cystitis (IC) is a syndrome of mystery in urology. IC is characterized by bladder pain associated with urgency, frequency, nocturia, dysuria and sterile urine.

Because the pathogenesis of IC remains unclear, the current goals of treatment are largely based on symptomatic relief. A certain percentage of patients treated have successful results in the short term, however, most patients experience symptom relapse in long-term follow-up and need continual treatment with several different therapeutic modalities. Therefore, surgical treatment aimed at decreasing bladder pain and increasing functional bladder capacity is the last stage treatment for patients with chronic IC which is refractory to conventional treatment modalities.

INTRAVESICAL BOTULINUM TOXIN A

Botulinum A toxin type A (BoNT-A) is an inhibitor of acetylcholine release at the presynaptic neuromuscular junction. Inhibition of acetylcholine release results in decreased regional muscle contractility at the injection sites. This chemical denervation is a reversible process, and axons resprout in about 3-6 months. Vanilloid receptors (VR1) are co-localized with purinergic receptor $P2X_3$, calcitonine gene-related peptide (CGRP), or substance P in the urothelium and suburothelial sensory fibers. In one study, a significant decrease was noted in $P2X_3$ immunoreactivity of the suburothelial fibers at 4 weeks after Botox injection with a further decrease in the responders of detrusor overactivity at 16 weeks [1]. The authors of that study speculated that Botox might reduce production/uptake of neurotrophic factors, and regulate expression of VR1 and/or $P2X_3$. In an animal model, Chuang et al found that intravesical Botox blocked acetic acid- induced bladder pain responses and inhibited CGRP release from afferent nerve terminals [2]. Intravesical Botox injections might not only reduce bladder sensitivity in patients with IC, but also induce desensitization in the central nervous system through affecting the overexpression of activated proteins in the dorsal horn ganglia [3]. Smith et al treated 13 IC patients with 100 U to 200 U of Dysport or Botox (Allergan, Irvine, CA, USA) injected submucosally in the trigone and bladder base and found that 69% of patients had subjective improvement. The symptom index improved by 71%, the problem index improved by 69% and bladder pain improved by 79%. They concluded that BoNT-A might have an antinociceptive effect on bladder afferent pathways in IC patients [4]. In another study, Kuo used suburothelial injections of 100 U BOTOX to treat 10 women with IC and improved results were reported in 7 3 months after injection. However, all patients with therapeutic effects had dysuria after treatment [5]. The functional bladder capacity recorded in a voiding diary significantly increased (155 ± 26.3 v 77 ± 27.1 mL, p=0.00) and the daily frequency (18 ± 7.7 v 24.2 ± 10.3, p=0.025) and pain score (2.4 ± 1.6 v 3.2 ± 1.1, p=0.003) significantly decreased 3 months after treatment. However, only cystometric capacity showed a significat increase (287 ± 115 v 210 ± 63.8 mL, p=0.05) in all urodynamic parameters. The author also noted that trigonal injections of an additional 100 U of BOTOX did not result in symptom or urodynamic improvement. Nevertheless, no adverse effects were reported.

The effects of Botox on IC patients were further confirmed by a recent study. Giannantoni et al treated 14 patients with injections of 200 U of BoNT-A in 20 mL saline at 20 sites in the trigone and bladder base. Twelve patients (85.7%) reported subjective improvement at 1 and 3 months, scores on the visual analog scale (VAS) for pain decreased, frequency decreased and bladder capacity increased significantly. Two patients reported dysuria and intermittent clean catheterization was needed [6]. In a long-term follow-up report from the same group, the beneficial effects persisted at 5 months in 26.6% of cases but daytime and nighttime urinary frequency increased and the pain score on a visual analog scale increased from baseline. At 12 months after treatment pain recurred in all patients. Nine patients complained of dysuria 1 month after treatment. Dysuria persisted in 4 cases at the 3-month follow-up and in 2 at the 5-month follow-up. The authors suggested that repeat BoNT-A injections were necessary in treating IC [7].

NEUROMODULATION

Sacral nerve stimulation is thought to act via stimulation of somatic afferents which inhibit the transmission of afferent messages arising from the bladder [8]. Therefore, sacral nerve stimulation has been applied to improve urgency, frequency, and urge incontinence as well as IC symptoms [9]. Peters et al found that sacral neuromodulation decreased narcotic requirements and subjective pelvic pain in 21 patients with refractory IC [10]. In another neuromodulation model, significant improvement in frequency, urgency and quality of life was noted in 51 women after posterior tibial nerve stimulation for 30 min weekly for 10 weeks [11]. In 33 women with IC, improvement in frequency, pain, voided volume, and bladder capacity was seen after percutaneous sacral nerve root stimulation [12]. Although the mechanisms of neuromodulation remain unclear, this therapeutic modality has been used to treat IC which is refractory to conventional therapies.

BLADDER AUGMENTATION AND CYSTECTOMY

Cystourethrectomy with urinary diversion or bladder augmenta-

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tion is the ultimate option for the treatment of refractory IC, particularly in patients with intractable pain. Lotenfoe et al achieved an overall success rate of 73% with cystourethrectomy and colonic urinary diversion [13]. They noted the success rate was 88% in patients with bladder capacities less than 400 mL, but only 20% in patients with capacities over 400 mL. These results raise the possibility that in some IC patients, the visceral pain might originate from central sensitization or psychological pain rather than the visceral organ itself.

ENTEROCYSTOPLASTY

Trigonal sparing orthotopic caecocystoplasty was reported effective in intractable IC after a 9-year follow-up. However, problems with complications such as de novo need for clean intermittent self-catheterization, recurrent symptoms, and carcinoma remain unsolved [14]. In another study, 14 of 18 patients treated with substitution enterocystoplasty (trigonal sparing) were pain free, 15 had resolution of dysuria and 12 could void spontaneously [15]. Bladder autoaugmentation has also been attempted in the treatment of refractory IC. Bladder autoaugmentation without cystectomy resulted in reduced bladder pain but only a limited increase in bladder capacity in long-term follow-up [Kuo HC, unpublished data].

MULTIMODAL THERAPY FOR IC

Since the etiology of IC is thought to be multi-factorial, multiple therapies might produce synergistic effects and better outcomes. Patients with moderate to severe disease may require a multimodal therapeutic approach using pentosan polysulphate (PPS) as a foundation, combined with antihistamines, analgesics, antispasmodics, or antidepressants. Patients with severe disease may require anesthetic instillation combined with PPS and sodium bicarbonate. Non-pharmacologic approaches, such as bladder training, biofeedback, and dietary changes can also provide supplementary relief, and should be added to the treatment of refractory IC [16]. For disease which is refractory to oral medication or intravesical instillation therapy, intravesical injection of BoNT-A or neuromodulation might provide a chance for symptomatic relief. In additional to different therapeutic options in different stages of IC, psychological support from peer groups and the medical team might also play an essential role in treating this vulnerable population. Invasive surgical treatment such as cystectomy or enterocystoplasty should only be used in severely distressed patients with disease refractory to all other treatments.

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